ARCHIVES
OF
THE MIDDLESEX HOSPITAL
VOLUME XV

# Eighth Report
FROM THE
Cancer Research Laboratories

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ARCHIVES

OF

THE MIDDLESEX HOSPITAL

VOLUME XV

Eighth Report

FROM THE

Cancer Research Laboratories

EDITED FOR THE CANCER INVESTIGATION COMMITTEE

BY

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(1908–1909).

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NOTICE.

In the following Pages, excepting where an asterisk (*) *is placed, or where the context makes it clear that such is not the case,* EVERY DIAGNOSIS OF MALIGNANT DISEASE HAS BEEN MADE AS THE RESULT OF MICROSCOPICAL EXAMINATION.

W. S. L.-B.

REPORTS
FROM THE
CANCER RESEARCH LABORATORIES

TABULATED SYNOPSES OF THE POST-MORTEM EXAMINATIONS AND OPERATIONS IN CASES OF MALIGNANT DISEASE DURING THE YEAR 1908.

By THE DIRECTOR and his ASSISTANTS.

In the following tables are given the results of all cases of malignant disease—as determined by microscopical examination—which were investigated in the Cancer Research Laboratories during the year 1908. The material was derived partly from the post-mortem room and partly from the operating theatre. In all 227 cases of malignant disease (males 70, females 157) have been examined microscopically. All of the above were in-patients. The total number of admissions to the Hospital as in-patients during 1908 was 3,938; viz., 1,856 males, and 2,082 females. In addition, 12 males and 41 females with malignant disease were admitted to the Electrical (Out-patient) Department for X-ray treatment. Histological examination was not made in these cases.

Besides the cases that have been mentioned, a certain number of patients were admitted (either to the general wards or to the special wards) in which the diagnosis was not made certain by histological examination. These are grouped in two classes according to the relative probability of accuracy in the diagnosis.

In the first group, the diagnosis was founded on naked-eye appearances or on touch, but the patients were either discharged unrelieved from the Hospital at their own request, or else left relieved after palliative operation (*e.g.*, cases of gastrostomy, colotomy, &c.).

In the second group the diagnosis was made upon clinical grounds alone.

GROUP I.

Cases diagnosed as Malignant Disease on Evidence derived from the Naked-Eye Appearance or Touch.

Site.	1908.		
	Males.	Females.	Total.
Breast	—	21	21
Uterus	—	15	15
Ovary	—	3	3
Bladder	2	—	2
Kidney	1	—	1
Mouth	2	1	3
Tongue	8	—	8
Sup. Maxilla	2	—	2
Tonsil	1	—	1
Stomach	7	2	9
Rectum	7	8	15
Omentum	1	1	2
Rodent Cancer	1	—	1
Skin	—	1	1
Neck (sarcoma)	3	—	3
Nose (sarcoma)	1	—	1
Nose (carcinoma)	1	—	1
Spine	1	1	2
Thyroid	—	1	1
Forehead (sarcoma)	1	—	1
Gall Bladder	1	—	1
Totals	40	54	94

GROUP II.

Cases diagnosed on Clinical Evidence only.

Site.	1908.		
	Males.	Females.	Total.
Œsophagus	7	2	9
Stomach	12	4	16
Prostate	7	—	7
Pancreas	4	4	8
Abdominal glands	2	—	2
Liver	3	1	4
Totals	35	11	46

TABLE I.—

—		Total.		26—30.		31—35.		36—40.		41—45.	
		M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
CARCINOMA.											
Cheek	Squamous	2	—	—	—	—	—	—	—	—	—
Face	Squamous	1	—	—	—	—	—	—	—	—	—
Sup. Maxilla	Squamous	1	—	—	—	—	—	—	—	—	—
Tongue	Squamous	9	—	—	—	—	—	1	—	2	—
Mouth	Squamous	1	—	—	—	—	—	—	—	—	—
Palate	Squamous	1	—	—	—	—	—	—	—	—	—
Œsophagus	Squamous	4	1	—	1	—	—	—	—	—	—
Stomach, Middle ...	Columnar	1	—	—	—	—	—	—	—	—	—
	Spheroidal	1	—	—	—	—	—	—	—	—	—
„ Pylorus ...	Spheroidal	1	1	—	—	—	—	1	—	—	—
Cæcum	Columnar	—	1	—	—	—	—	—	—	—	—
Colon	Columnar	3	1	—	—	—	—	—	—	—	—
Sigmoid Flexure ...	Columnar	1	1	—	—	—	—	—	—	—	—
Rectum	Spheroidal	—	1	—	—	—	—	—	—	—	—
	Columnar	5	5	—	—	—	1	—	—	2	—
Anus	Squamous	—	1	—	—	—	—	—	—	—	1
Liver	Spheroidal	2	2	—	—	—	—	—	—	—	—
Pancreas	Columnar	—	1	—	—	—	—	—	—	—	—
	Spheroidal	—	2	—	—	—	—	—	—	—	1
Peritoneum	Colloid	—	1	—	—	—	—	—	—	—	—
Bladder	Transitional	1	—	—	—	—	—	—	—	—	—
	Squamous	1	1	—	—	—	—	—	—	—	—
Urethra	Squamous	—	1	—	—	—	—	—	—	—	—
Prostate	Spheroidal	2	—	—	—	—	—	—	—	—	—
Ovary ...	Malignant cystadenoma	—	2	—	—	—	—	—	—	—	1
Cervix uteri	Squamous	—	14	—	1	—	1	—	3	—	2
Vulva	Squamous	—	2	—	—	—	—	—	—	—	—
Breast	Spheroidal	—	21	—	—	—	1	—	1	—	2
SARCOMA.											
Mixed-cell		2	1	—	—	—	—	—	—	—	—
Small round-cell		—	1	—	—	—	—	—	—	—	—
Lymphosarcoma		1	—	—	—	—	—	medi-astinum	—	—	—
ENDOTHELIOMA		—	8	—	—	—	uterus 2	—	—	—	uterus
		40	69								

Post-mortem Cases.

46—50.		51—55.		56—60.		61—65.		66—70.		71—75.		76—80.	
M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
—	—	—	—	—	—	1	—	1	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	1	—	—	—
—	—	1	—	—	—	—	—	—	—	—	—	—	—
2	—	1	—	1	—	—	—	2	—	—	—	—	—
1	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	1	—	—	—	—	—	—	—	—	—
—	—	—	—	1	—	2	—	1	—	—	—	—	—
1	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	1	—	—	—	—	—	—	—	—	—
—	—	—	1	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	1	—	—	—	—	—	—	—	—
—	—	—	—	2	1	—	—	1	—	—	—	—	—
—	—	—	—	—	—	1	1	—	—	—	—	—	—
—	1	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	1	2	1	1	2	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	1	1	1	1	—	—	—	—	—	—	—	—	—
—	—	—	1	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	1	—	—	—	—	—	—	—	—
—	1	—	—	—	—	—	—	—	—	—	—	—	—
1	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	1	—	—	—	—	1	—	—	—	—
—	—	—	1	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	1	—	1	—	—	—	—	—
—	—	—	—	—	—	—	1	—	—	—	—	—	—
—	2	—	2	—	2	—	—	—	—	—	—	—	1
—	—	—	—	—	—	—	1	—	1	—	—	—	—
—	3	—	3	—	5	—	4	—	1	—	1	—	—
—	—	testis	—	adrenal	kidney	—	—	—	—	—	—	—	—
—	—	—	pancreas.	—	—	—	—	—	—	—	—	—	—
—	—	-	—	—	—	—	—	—	—	—	—	-	—
—	uterus 2	—	—	—	breast	—	—	—	-	-	orbit	—	breast

TABLE II.—

—	Total.		11—15.		16—20.		21—25.		26—30.		31—35.		36—40.	
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
CARCINOMA.														
Upper Jaw ... Squamous	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Lip ... ... Squamous	3	—	—	—	—	—	—	—	—	—	—	—	—	—
Tongue ... ... Squamous	10	1	—	—	—	—	—	—	1	—	—	—	—	—
Mouth ... ... Squamous	1	—	—	—	—	—	—	—	—	—	—	—	—	—
Palate ... ... Squamous	1	—	—	—	—	—	—	—	—	—	—	—	—	—
Stomach ... ... Columnar	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Intestine ... ... Columnar	1	4	—	—	—	—	—	—	—	—	—	—	sigmoid	—
Uro-genital System Squamous	2	5	—	—	—	—	—	—	—	—	—	—	—	—
Uro-genital System Spheroidal	—	1	—	—	—	—	—	—	—	—	—	corpus uteri	—	—
Uro-genital System Columnar	—	7	—	—	—	—	—	—	—	—	—	—	—	—
Breast Spheroidal	1	46	—	—	—	—	—	—	—	—	—	1	—	5
Breast Columnar	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Other Sites ... Squamous	1	1	—	—	—	—	—	—	—	—	—	—	—	—
RODENT CANCER	3	1	—	—	—	—	—	—	1	—	—	—	—	—
SARCOMA.														
Mixed-cell	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Round-cell	2	2	—	—	—	—	—	—	—	—	—	—	—	—
Spindle-cell	1	1	femur	—	—	—	—	—	—	—	—	—	—	ovary
Myeloid	—	1	—	—	—	—	—	—	—	—	—	—	—	jaw
Lymphosarcoma	1	—	—	—	cervical glands	—	—	—	—	—	—	—	—	—
ENDOTHELIOMA	1	6	—	—	—	—	—	—	—	—	—	—	—	—
DOUBTFUL	2	12	—	—	skin	—	parotid	breast	—	—	—	—	—	breast
	30	92	TOTAL NUMBER OF HOSPITAL OPERATION CASES FOR MALIGNANT DISEASE	Carcinoma—Males 23, Females 69 Sarcoma „ 4, „ 5 Endothelioma „ 1, „ 6 Doubtful „ 2, „ 12											
NON-MALIGNANT.	15	23	—	—	2	1	1	4	1	5	—	1	—	3
	45	115	TOTAL NUMBER OF HOSPITAL OPERATION CASES EXAMINED IN CANCER RESEARCH LABORATORIES.												

Operation Cases.

41—45.		46—50.		51—55.		56—60.		61—65.		66—70.		71—75.		76—80.		81—85.	
M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—	1	—
—	—	—	—	2	—	3	1	1	—	2	—	1	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—
—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	rectum	—	rectum sigmoid	—	—	—	colon	—	—	—	—	—	—	—	—	—	—
—	vulva	bladder	vulva	—	cervix uteri	penis	cervix uteri	—	bladder	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	fundus uteri	—	fundus uteri, ovary	—	uterus ovary	—	fundus uteri	—	ovary	—	—	—	—	—	—	—	—
—	10	—	9	—	5	1	6	—	5	—	3	—	1	—	—	—	1
—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	scalp	—	—	—	—	gall-bladder	—	—	—	—	—	—
—	—	—	1	—	—	—	—	—	—	—	—	—	2	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	breast	—	—	—	—
pharynx	—	—	thyroid	—	—	—	—	orbit	—	—	—	—	breast	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
—	breast(2) ovary	pharynx	breast	—	breast (2)	—	—	—	—	—	—	—	—	—	—	—	—
—	parotid breast(2) skin abdomen	—	cervix uteri	—	breast cervix uteri	—	breast cervix uteri	—	—	—	—	—	—	—	—	—	—
1	2	2	3	1	2	2	1	3	1	—	—	2	—	—	—	—	—

TABLE III.

SYNOPSES OF POST-MORTEM CASES.

CARCINOMATA.

No	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
1	H.R.C. 161/08	M	63	Squamous cell carcinoma of cheek.	Liver.	... ...	(ii) Well nourished.	(i) 25 April '08. (ii) 5 Aug. '08.
2	T.B. 223/08	M	67	Squamous cell carcinoma of cheek.	Cervical glands.	... ...	(ii) Emaciated.	(i) 28 Sept. '08. (ii) 19 Oct. '08.
3	J.O. 41/08	M	72	Squamous cell carcinoma of face.	Submaxillary and carotid glands.	Intra-hepatic calculus.	(ii) Emaciated.	(i) 6 Feb. '08. (ii) 24 Feb. '08.
4	R.A. 85/08	M	51	Squamous cell carcinoma of upper jaw.	None.	Bronchitis.	(ii) Much emaciated.	(i) 14 Sept. '07. (ii) 23 April '08. (iii) Excision of jaw
5	E.S.B. 252/08	M	36	Squamous cell carcinoma of tongue.	Submaxillary glands.	... ...	(ii) Great emaciation.	(i) 9 Sept. '08. (ii) 15 Nov. '08.
6	T.R. 264/08	M	44	Squamous cell carcinoma of tongue.	None.	Double pleural effusion. Ascites.	(ii) Great emaciation.	(i) 29 Nov. '07. (ii) 27 Nov. '08
7	J.B. 204/08	M	45	Squamous cell carcinoma of tongue.	Submaxillary and cervical glands.	... ...	(ii) Emaciated.	(i) 31 Aug. '08. (ii) 23 Sept. '08.
8	A.B. 5/08	M	46	Squamous cell carcinoma of tongue.	R. cervical and submaxillary glands.	Double broncho-pneumonia.	(ii) Emaciated.	(i) 18 Nov. '07. (ii) 18 Jan. '08.

9	G.C.C. 98/08	M	48	Squamous cell carcinoma of floor of mouth.	Submaxillary glands.	... ...	(ii) Emaciated.	(i) 4 May '08. (ii) 14 May '08.
10	F.T. 174/08	M	50	Squamous cell carcinoma of tongue.	None.	Mitral stenosis.	(ii) Great emaciation.	(i) 23 Dec. '07. (ii) 27 Aug. '08.
11	H.F. 255/08	M	53	Squamous cell carcinoma of tongue.	Lung, submaxillary glands.	... ...	(ii) Emaciated.	(i) 20 Oct. '08. (ii) 20 Nov. '08.
12	F.C. 220/08	M	57	Squamous cell carcinoma of tongue.	Heart.	Chronic peritonitis.	... ...	(i) 9 Jan. '08. (ii) 15 Oct. '08.
13	R.P. 32/08	M	66	Squamous cell carcinoma of tongue.	* Carotid glands.	... ...	(ii) Emaciated.	(i) 15 July '07. (ii) 18 Feb. '08.
14	J.B. 172/08	M	69	*Squamous cell carcinoma of tongue.	*Cervical glands.	Marked atheroma of aorta and coronary arteries.	(ii) Emaciated.	(i) 27 Feb. '08. (ii) 21 Aug. '08.
15	D.A. 278/08	M	60	Squamous cell carcinoma of palate.	Salivary gland.	... ...	(ii) Much emaciation.	(i) 18 Dec. '08. (ii) 21 Dec. '08.
16	G.B. 241/08	F	27	Squamous cell carcinoma of œsophagus (upper end).	Pleuræ, pericardium.	... ...	(ii) Emaciated.	(i) 17 March '08. (ii) 8 Nov. '08. (iii) Gastrostomy Tracheotomy.
17	J.G. 211/08	M	69	Squamous cell carcinoma of œsophagus (upper end).	None.	... ...	(ii) Well nourished. Hosp. p.m. 172.	(i) 17 Sept. '08. (ii) 28 Sept. '08. (iii) Gastrostomy.
18	W.G. 48/08	M	56	Squamous cell carcinoma of œsophagus (middle third).	Mediastinal glands.	Broncho-pneumonia.	(ii) Body thin. Hosp. p.m. 46.	(i) 6 Jan. '08. (ii) 1 March '08. (iii) Gastrostomy.
19	C. 81/08	M	65	Squamous cell carcinoma of œsophagus (middle third).	Liver, mediastinal glands.	Broncho-pneumonia.	(ii) Well nourished. Hosp. p.m. 81.	(i) 14 April '08. (ii) 16 April '08. (iii) Gastrostomy.
20	G.P. 158/08	M	65	Squamous cell carcinoma of œsophagus (lower third).	None.	Broncho-pneumonia.	(ii) Emaciated. Hosp. p.m. 143.	(i) 15 March '08. (ii) 5 Aug. '08.

Table III.—Synopses of Post-mortem Cases—*cont.*

No.	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
21	T.G. 77/08	M	47	Columnar cell carcinoma of stomach (body).	Portal glands.	... ...	(ii) Great emaciation. Hosp. p.m. 76.	(i) 30 March '08. (ii) 13 April '08.
22	J.B. 9/08	M	58	Spheroidal cell carcinoma of stomach (small curvature).	Liver.	General peritonitis.	(ii) Emaciated. Hosp. p.m. 23.	(i) 1 Nov. '07. (ii) 27 Jan. '08.
23	C.H.P. 21/08	M	38	Spheroidal cell carcinoma of pylorus.	Skin, liver, peritoneum; portal, lumbar, pancreatic and bronchial glands.	Bronchitis.	(ii) Emaciated.	(i) 8 Jan. '08. (ii) 6 Feb. '08. (iii) Gastro-jejunostomy.
24	E.J. 209/08	F	52	Spheroidal cell carcinoma of pylorus.	Aortic glands.	Umbilical hernia.	(ii) Well nourished.	(i) 24 Sept. '08. (ii) 2 Oct. '08.
25	S.S. 187/08	F	56	Columnar cell carcinoma of cæcum.	None (abdomen only examined).	... ...	(ii) Body thin. Hosp. p.m. 159.	(i) 30 July '08. (ii) 7 Sept. '08.
26	E.T. 31/08	F	58	Columnar cell carcinoma of colon.	None.	General peritonitis.	... ... Hosp. p.m. 35.	(i) 10 Feb. '08. (ii) 14 Feb. '08. (iii) Colotomy, laparotomy.
27	G.A. 127/08	M	60	Columnar cell carcinoma of transverse colon.	* Liver.	Old pulmonary tuberculosis. General peritonitis.	... ... Hosp. p.m. 120.	(i) 7 June '08. (ii) 26 June '08. (iii) Laparotomy, R. inguinal colotomy
28	T.H. 215/08	M	60	Columnar cell carcinoma of colon.*	Liver.	... ...	(i) Meckel's diverticulum. (ii) Emaciated. Hosp. p.m. 181.	(i) 6 Oct. '08. (ii) 9 Oct. '08. (iii) Colotomy.

29	J.H.M 208/08	M	66	Columnar cell carcinoma (colloid) of colon.	None.	... ...	(ii) Well nourished. Hosp. p.m. 174.	(i) 21 Sept. '08. (ii) 29 Sept. '08. (iii) Colotomy.
30	C.G. 153/08	F	62	Columnar cell carcinoma of sigmoid.	Liver, left kidney.	... ...	(ii) Body stout. Hosp. p.m. 139.	(i) 5 July '08. (ii) 28 July '08. (iii) Colotomy.
31	J.M. 118/08	M	63	Columnar cell carcinoma of sigmoid.	None.	... ...	(ii) Body thin. Hosp. p.m. 111.	(i) 8 June '08. (ii) 12 June '08. (iii) Left inguinal colotomy.
32	M.L. 171/08	F	35	Columnar cell carcinoma of rectum.	None (abdomen only examined).	... ...	(ii) Well developed. Hosp. p.m. 152.	(i) 18 Aug. '08. (ii) 18 Aug. '08.
33	A.D. 16/08	M	42	Columnar cell carcinoma of rectum.	Lungs, liver, right kidney, left adrenal, iliac glands.	L. hydronephrosis. Cystitis.	(ii) Moderately nourished.	(i) 21 Jan. '08. (ii) 3 Feb. '08. (iii) Left inguinal colotomy.
34	T.P. 97/08	M	45	Columnar cell carcinoma of rectum.	None.	... ...	(ii) Emaciated. Hosp. p.m. 94.	(i) 13 Mar. '08. (ii) 9 May '08.
35	C.G. 107/08	F	46	Spheroidal cell carcinoma of rectum.	Lumbar glands, peritoneum.	Cystadenoma of ovary.	(ii) Emaciated.	(i) 28 April '08. (ii) 24 May '08. (iii) Left inguinal colotomy.
36	E.C. 43/08	F	59	Columnar cell carcinoma of rectum.	Liver, lumbar glands.	Fatty heart. General peritonitis.	(ii) Body stout.	(i) 16 Jan. '08. (ii) 25 Feb. '08. (iii) Left inguinal colotomy.
37	W.M. 60/08	M	62	Columnar cell carcinoma of rectum.	Liver.	General peritonitis.	(ii) Well nourished. Hosp. p.m. 65.	(i) 17 March '08. (ii) 23 March '08. (iii) Excision of rectum.
38	E.T. 112/08	F	64	Columnar cell carcinoma of rectum.	Inguinal glands.	Double hydronephrosis.	(ii) Emaciated.	(i) 10 Aug. '07. (ii) 3 May '08.

TABLE III.—SYNOPSES OF POST-MORTEM CASES—*cont.*

No.	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
39	F.H.L. 195/08	M	65	Columnar cell carcinoma of rectum.	None.	Old pulmonary tuberculosis. Tuberculous disease of left kidney.	(ii) Emaciated. Hosp. p.m. 162.	(i) 9 Sept. '08. (ii) 12 Sept. '08. (iii) Colotomy.
40	A.J.B. 54/08	M	66	*Columnar cell carcinoma of rectum.	Liver.	L. hydronephrosis.	(ii) Much emaciated.	(i) 6 Feb. '08. (ii) 12 March '08.
41	J.R. 30/08	F	66	Columnar cell carcinoma of rectum.	Liver.	General peritonitis.	(ii) Well nourished. Hosp. p.m. 34.	(i) 28 Jan. '08. (ii) 13 Feb. '08. (iii) Colotomy, laparotomy.
42	C.R. 14/08	F	67	Columnar cell carcinoma of rectum.	Thyroid, pancreas, inguinal glands.	R. pyonephrosis.	(ii) Much emaciated.	(i) 19 Sept. 07. (ii) 31 Jan. '08. (iii) Left inguinal colotomy.
43	A.C. 100/08	F	42	Squamous cell carcinoma of anus.	None.	... ...	(ii) Emaciated.	(i) 30 Dec. '07. (ii) 15 May '08.
44	E.S. 99/08	F	48	Spheroidal cell carcinoma of liver.	Lung, pleura, diaphragm, adrenals, mesenteric glands.	Jaundice.	(ii) Much emaciated.	(i) 7 Mar. '08. (ii) 14 May '08. (iii) Laparotomy.
45	F.H. 135/08	M	52	(?) Spheroidal cell carcinoma of liver.	Lung.	Ascites.	... ... Hosp. p.m. 122.	(ii) 2 July '08.
46	S.G. 234/08	F	53	Spheroidal cell carcinoma of liver.	Abdominal glands, lungs, thyroid.	... ...	(ii) Body fat. Hosp. p.m. 193.	(i) 17 Oct. '08. (ii) 29 Oct. '08. (iii) Laparotomy.
47	G.B. 121/08	M	56	Spheroidal cell carcinoma of liver.	None.	Ascites.	(ii) Body thin. Hosp. p.m. 115.	(i) 16 Jan. '08. (ii) 16 June '08.

48	J.S. 59/08	F	45	Spheroidal cell carcinoma of pancreas.	* Liver, peritoneum; cervical, bronchial, and mesenteric glands.	Jaundice. Ascites.	(ii) Very emaciated.	(i) 1 Dec. '07. (ii) 22 March '08.
49	E.C. 17/08	F	55	Columnar cell carcinoma of pancreas.	Liver.	Jaundice. Chronic peritonitis.	(ii) Great emaciation. Hosp. p.m. 29.	(i) 30 Oct. '07. (ii) 3 Feb. '08. (iii) Laparotomy.
50	E.S. 271/08	F	57	Spheroidal cell carcinoma of head of pancreas.	Aortic glands.	Jaundice.	(ii) Emaciated. Hosp. p.m. 214.	(i) 9 Nov. '08. (ii) 7 Dec. '08.
51	R.P 3/08.	F	50	Colloid carcinoma of peritoneum.	Inguinal glands.	Pleural effusion.	(ii) Emaciated.	(i) 20 Nov. '07. (ii) 6 Jan. '08.
52	W.P. 87/08	M	47	Transitional cell carcinoma of bladder.	None.	... ...	(ii) Body thin. Hosp. p.m. 87.	(i) 11 March '08. (ii) 25 April '08.
53	C.R. 173/08	M	59	? Squamous cell carcinoma of bladder.	None.	Double pyonephrosis.	(ii) Emaciated. Hosp. p.m. 155.	(i) 24 Aug. '08. (ii) 26 Aug. '08.
54	E.F. 186/08	F	70	Squamous cell carcinoma of bladder.	None.	Chronic peritonitis. Hydro- and pyonephrosis.	(ii) Great emaciation.	(i) 26 Oct. '08. (ii) 27 Nov. 08.
55	E.F. 186/08	F	54	Squamous cell carcinoma of urethra.	Lung, pleura; iliac and inguinal glands.	Gallstones.	(ii) Body very fat.	(i) 15 Aug. '08. (ii) 4 Sept. '08.
56	R.F. 222/08	M	65	Spheroidal cell carcinoma of prostate.	R. fibula.	Consecutive nephritis.	(ii) Emaciated.	(i) 27 May '07. (ii) 19 Oct. '08.
57	J.B. 229/08	M	68	Spheroidal cell carcinoma of prostate.	Skull.	Broncho-pneumonia.	(ii) Well nourished. Hosp. p.m. 191.	(i) 25 Oct. '08. (ii) 26 Oct. '08.
58	E.I 55/08	F	45	Malignant cystadenoma of ovary.	None.	Thyroid cysts.	(i) Pyramidal lobe of thyroid well marked. (ii) Emaciated.	(i) 30 Aug. '06. (ii) 15 March '08.

TABLE III.—SYNOPSES OF POST-MORTEM CASES—*cont.*

No.	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
59	E.A. 8/08	F	63	Papilliferous cystadenoma of ovary.	Peritoneum, lumbar glands.	Ascites. Pleural effusion. Erysipelas of face.	... ...	(i) 2 Nov. '07. (ii) 23 Jan. '08.
60	A.T. 23/08	F	30	Squamous cell carcinoma of cervix uteri.	Iliac glands.	Double hydronephrosis. Vesico-vaginal fistula. Purulent peritonitis.	(ii) Emaciated.	(i) 14 Dec. '07. (ii) 8 Feb. '08.
61	M.C. 93/08	F	34	Squamous cell carcinoma of cervix uteri.	Lumbar glands.	... ...	(ii) Extremely emaciated.	(i) 7 Jan. '08. (ii) 29 April '08.
62	L.K. 154/08	F	37	Squamous cell carcinoma of cervix uteri.	None.	... ...	(ii) Well nourished.	(i) 8 May '08. (ii) 29 July '08.
63	F.S. 24/08	F	39	*Carcinoma of cervix uteri.	None.	Double pyonephrosis.	(ii) Emaciated.	(i) 8 Oct. '07. (ii) 9 Feb. '08.
64	A.S.W. 116/08	F	40	Squamous cell carcinoma of cervix uteri.	None.	Double hydronephrosis.	(ii) Emaciated.	(i) 6 June '08. (ii) 15 June '08. (iii) Laparotomy.
65	K.A. 40/08	F	43	Squamous cell carcinoma of cervix uteri.	Lumbar glands.	Pleural effusions. Old syphilitic scars on face, trunk, limbs and tongue.	(ii) Well nourished.	(i) 19 July '07. (ii) 21 Feb. '08.
66	I.J. 123/08	F	45	Squamous cell carcinoma of cervix uteri.	Aortic glands.	Old tubercle in lungs. General peritonitis. Septic nephritis.	(ii) Greatly emaciated.	(i) 4 Nov. '07. (ii) 21 June '08.
67	E.R. 106/08	F	46	Squamous cell carcinoma of cervix uteri.	None.	Pyonephrosis. Multiple abscesses in liver and kidneys. Pericarditis. Broncho-pneumonia.	(ii) Body thin. Hosp. p.m. 102.	(i) 19 May '08. (ii) 23 May '08.

68	E.H. 272/08	F	47	Squamous cell carcinoma of cervix uteri.	Aortic gland.	... ...	(ii) Emaciated.	(i) 17 March '08. (ii) 6 Dec. '08.
69	J.T. 76/08	F	52	Squamous cell carcinoma of cervix uteri.	None.	Hydatid of liver. R. pyonephrosis.	(ii) Emaciated.	(i) 13 Feb. '08. (ii) 12 April '08.
70	E.W. 79/08	F	54	*Carcinoma of cervix uteri.	None.	... ...	(ii) Well nourished.	(i) 24 Dec. '07. (ii) 13 April '08.
71	M.A.W. 75/08	F	56	Squamous cell carcinoma of cervix uteri.	None.	Pyonephritis.	(ii) Emaciated.	(i) 15 March '08. (ii) 11 April '08.
72	I.E.J. 89/08	F	57	Squamous cell carcinoma of cervix uteri.	None.	Double hydronephrosis.	(ii) Much emaciated.	(i) 14 May '07. (ii) 27 April '08.
73	S.B. 203/08	F	76	Squamous cell carcinoma of cervix uteri.	Lumbar glands.	Gallstones.	(ii) Emaciated.	(i) 13 June '08. (ii) 23 Sept. '08.
74	H.M.H. 94/08	F	61	Squamous cell carcinoma of vulva.	R. inguinal glands.	Œdema of legs. Chronic ulcer of stomach. R. hydronephrosis.	(ii) Emaciated.	(i) 13 Jan. '08. (ii) 29 April '08.
75	M.E.P. 162/08	F	69	Squamous cell carcinoma of vulva.	None.	Adherent pericardium. Renal calculi. Serous cyst in liver. Cystitis.	(ii) Extreme emaciation.	(i) 27 Sept. '07. (ii) 6 Aug. '08.
76	E.K. 111/08	F	35	Spheroidal cell carcinoma of right breast.	None.	Jaundice.	(ii) Emaciated.	(i) 22 April '08. (ii) 2 June '08.
77	L.E.V. 42/08	F	36	Spheroidal cell carcinoma of left breast.	Thyroid, lung.	Œdema of left arm. Double pleural effusion.	... ...	(i) 25 Dec. '07. (ii) 25 Feb. '08.
78	C.S. 44/08	F	44	Spheroidal cell carcinoma of both breasts.	Liver, skull, spine.	Fractures of both humeri.	(ii) Emaciated.	(i) 24 June '07. (ii) 25 Feb. '08. (iii) Amputation of both breasts.
79	E.H. 261/08	F	45	Spheroidal cell carcinoma of right breast.	Portal glands, liver.	Jaundice. Atheroma.	(ii) Much emaciation.	(i) 16 Nov. '08. (ii) 23 Nov. '08. (iii) Amputation of breast.

TABLE III.—SYNOPSES OF POST-MORTEM CASES—*cont.*

No.	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
80	E.C. 265/08	F	48	Spheroidal cell carcinoma of right breast.	L. breast, liver; axillary and portal glands.	L. pleural effusion.	(ii) Well nourished.	(i) 15 July '08. (ii) 29 Nov. '08.
81	E.B. 83/08	F	49	Spheroidal cell carcinoma of left breast.	Pleura, skin.	... ...	(ii) Body stout.	(i) 20 Nov. '07. (ii) 20 April '08. (iii) Amputation of breast.
82	M.A.F. 1/08	F	49	Spheroidal cell carcinoma of right breast.	Liver, mesenteric glands.	Œdema of right arm. Pleural effusion.	... ...	(i) 16 Oct. '07. (ii) 1 Jan. '08.
83	C.S. 144/08	F	51	Spheroidal cell carcinoma of right breast.	Left breast*, liver, lung.	Œdema of right arm. R. pleural effusion. Ascites.	(ii) Well nourished.	(i) 22 April '08. (ii) 12 July '08.
84	M.N. 58/08	F	53	Spheroidal cell carcinoma of right breast.	L. breast, liver, muscle; axillary and inguinal glands.	Œdema of right arm.	(ii) Rather emaciated.	(i) 19 Feb. '08. (ii) 22 March '08. (iii) Lymphangioplasty.
85	C.T. 210/08	F	54	Spheroidal cell carcinoma of right breast.	Lungs, bronchial glands.	Gallstones.	(ii) Well nourished.	(i) 3 Oct. '08. (ii) 3 Oct. '08.
86	L.W. 115/08	F	56	Spheroidal cell carcinoma of right breast.	Lungs, rib, bronchial glands.	R. pleural effusion. Gallstones.	(ii) Emaciated.	(i) 18 Jan. '08. (ii) 10 May '08. (iii) Lymphangioplasty.
87	E.A. 270/08	F	57	Spheroidal cell carcinoma of left breast.	Humerus, sternum, orbit.	... ...	(ii) Well nourished.	(i) 3 Jan. '08. (ii) 5 Dec. '08.
88	M.K. 155/08	F	58	Spheroidal cell carcinoma of right breast.	Pleura.	Œdema of right arm.	(ii) Well nourished.	(i) 14 July '08. (ii) 29 July '08.

89	E.K. 82/08	F	59	Spheroidal cell carcinoma of right breast.	Lung, pleura.	L. hydronephrosis.	(ii) Greatly emaciated.	(i) 15 April '08. (ii) 20 April '08.
90	E.B. 74/08	F	60	Spheroidal cell carcinoma of left breast.	R. breast, lungs, pancreatic gland.	... ...	(ii) Emaciated.	(i) 9 Nov. '07. (ii) 12 April '08. (iii) Amputation of breast.
91	L.D. 262/08	F	61	Spheroidal cell carcinoma of left breast.	Pleuræ, diaphragm, kidney.	Pleural effusion.	(ii) Much emaciated.	(i) 14 Oct. '08. (ii) 23 Nov. '08.
92	M.C. 49/08	F	61	Spheroidal cell carcinoma of right breast.	Liver, skin.	R. pleural effusion.	(ii) Much emaciated.	(i) 24 Feb. '08. (ii) 4 Mar. '08. (iii) Amputation of breast.
93	E.B. 277/08	F	61	Spheroidal cell carcinoma of right breast.	Pericardium, intestines.	... ...	(ii) Well nourished.	(i) 3 Dec. '08. (ii) 20 Dec. '08. (iii) Amputation of breast.
94	E.A.McD. 102/08	F	65	Spheroidal cell carcinoma of right breast.	Thyroid, lung, intestine; cervical and bronchial glands.	R. pleural effusion.	(ii) Emaciated.	(i) 24 March '08. (ii) 15 May '08. (iii) Amputation of breast.
95	E.E. 212/08	F	68	Spheroidal cell carcinoma of left breast.	R. breast, aortic glands, tissues of neck.	Chronic peritonitis.	(ii) Emaciated.	(i) 30 July '08. (ii) 8 Oct. '08.
96	J.I. 243/08	F	73	Spheroidal cell carcinoma of right breast.	Thyroid, pleura; axillary and lumbar glands.	Gallstones.	(ii) Much emaciation.	(i) 30 April '07. (ii) 10 Nov. '08.

TABLE III.—SYNOPSES OF POST-MORTEM CASES—*cont.*

SARCOMATA.

No.	Initials and Cancer Register Number.	Sex.	Age at Death.	Nature of new growth and part primarily affected.	Sites of Secondary new growth.	Other morbid changes present.	(i.) Congenital abnormalities. (ii.) General remarks.	(i.) Date of admission. (ii.) Date of death. (iii.) Surgical operation, if any.
1	J.W.S. 92/08	M	54	Mixed cell sarcoma of testicle.	Inguinal and abdominal glands.	Pyonephritis.	(ii) Much emaciated.	(i) 14 Mar. '08. (ii) 28 Apr. '08.
2	J.A. 2/08	F	56	Mixed cell sarcoma of left kidney.	R. kidney, liver, spleen, bladder, heart, lungs, thyroid, diaphragm, mesentery, pectoral muscle, abdominal lymph glands.	... ...	(ii) Much emaciated.	(i) 28 Dec. '07. (ii) 4 Jan. '08.
3	M.A.M. 156/08	F	58	Mixed cell sarcoma of right adrenal.	None.	Chronic peritonitis.	(ii) Emaciated.	(i) 19 Nov. '07. (ii) 4 Aug. '08. (iii) Colotomy.
4	M.S. 200/08	F	52	? Small round cell sarcoma of pancreas.	Liver.	Gallstones.	(ii) Well nourished. Hosp. p.m. 165.	(i) 12 Sept. '08. (ii) 21 Sept. '08.
5	T.J. 138/08	M	39	Lympho-sarcoma of mediastinum.	None.	... ...	(ii) Well nourished. Hosp. p.m. 125.	(i) 13 May '08. (ii) 6 July '08.
				ENDOTHELIOMATA.				
1	E.M. 133/08	F	32	Endothelioma of uterus.	Lung, liver, kidney, ovary, heart, omentum, vena cava, *lumbar glands.	Œdema of legs. Pulmonary tuberculosis. Pyonephrosis.	(ii) Emaciated.	(i) 1 May '08. (ii) 1 July '08.
2	A.K.E. 143/08	F	34	Endothelioma of cervix uteri.	Omentum.	... ...	(ii) Emaciated.	(i) 26 Mar. '08. (ii) 10 July '08.

3	M.C. 136/08	F	44	Endothelioma of cervix uteri.	Liver, capsule of spleen.	General peritonitis. Double pyelonephritis. Old pulmonary tubercle.	(ii) Much emaciated.	(i) 12 June '08. (ii) 3 July '08. (iii) Laparotomy.
4	S.W. 202/08	F	47	Endothelioma of cervix uteri.	L. adrenal, lumbar glands.	... ...	(ii) Emaciated.	(i) 25 Aug. '08. (ii) 23 Sept. '08.
5	E.A. 141/08	F	50	Endothelioma of cervix uteri.	Lumbar glands.	R. pleural effusion. Double hydronephrosis.	(ii) Well nourished.	(i) 24 March '08. (ii) 9 July '08.
6	E.W. 279/08	F	56	Endothelioma of left breast.	Clavicle, skull, liver, lung; mediastinal and mesenteric glands.	... ...	(ii) Body thin. Hosp. p.m. 219.	(i) 28 Nov. '08. (ii) 21 Dec. '08.
7	H.M. 266/08	F	73	Endothelioma of orbit.	None.	... ...	(ii) Emaciated.	(i) 24 June '08. (ii) 1 Dec. '08.
8	U.H. 170/08	F	76	Endothelioma of left breast.	Sternum, skull, liver, pleura,*	Mitral stenosis.	(ii) Much emaciation.	(i) 4 Aug. '08. (ii) 12 Aug. '08.

MALIGNANT DISEASE OF THE CERVIX UTERI. A STATISTICAL STUDY BASED ON THE RECORDS OF THE MIDDLESEX HOSPITAL FROM 1904–8 INCLUSIVE.

By H. MacCORMAC.

In this paper an attempt has been made to deal with 241 cases of carcinoma of the cervix uteri, a survey of practically all such admitted into the general or cancer wards of the Middlesex Hospital during the quinquennium 1904–8.

W. L. Andriezen and A. Leitch * have published statistics of cases previously recorded, from the earliest days of the charity up to 1903; their paper also included statistics of cancer of the body of the womb, and of the vagina and vulva. It was desired to analyse all these sites of cancerous disease in the present paper, but during the years dealt with data sufficient for accurate figures had not accumulated. For this reason only cervical disease has been examined.

In the 241 cases investigated, every point under analysis was not recorded in the notes every time. Therefore, the total is not arrived at under any one heading, and indeed often falls far short of it. For this reason, the number used to obtain any percentage will be always stated.

GENERAL.

Civil Condition and Fertility.—Details were given in 237 instances. Of these 224 had married, and 13 remained single —a percentage of 5·5 for unmarried women. It was further found that out of 220 married women, 198 had borne children, 8 had become pregnant but had aborted, and 14 only had been quite sterile.

Heredity.—Any family history of cancer was denied by 142 women, while 36 admitted cancerous, and 37 tuberculous, relatives. In 7 instances there was a history of both diseases.

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* Archives of Middlesex Hospital. Fifth Cancer Report.

Age at Onset.—Such a factor can only be approximate, because by onset of disease is meant onset of the first noticeable symptom. In 234 cases details were available, and amongst them the illness declared itself at an average age of 46·15 years. The youngest patient was 24, the oldest 75; in both the clinical findings were confirmed by microscopical evidence.

TABLE I.

Giving the Number of Cases beginning during the various Quinquennial Age-Periods.

Age	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79
Number of cases...	1	4	23	37	44	39	40	24	13	3	3	3
Average age at onset.	24·00	28·00	32·13	37·02	42·25	47·33	52·12	56·37	61·76	65·66	71·33	74·43
Percentage ...	0·43	1·71	9·83	15·81	18·80	16·67	17·09	10·26	5·56	1·28	1·28	1·28

The above table suggests that a cervical carcinoma begins most often between the ages of 40 and 44. These figures are quite in agreement with those of Andriezen and Leitch.

While this table may be accurate enough for women under 44 years, it is not so for the later age-periods; the number of females alive is then steadily becoming less from other causes.

To get an absolute, instead of a relative, set of figures, the population from which the above given cases were drawn should be obtained; a percentage estimate could then be got for different age-periods. While such a method is proper in theory, in practice it obviously cannot be carried out. It therefore becomes necessary to take a large sample of the female population and find how many survive at each succeeding age-period. In Newsholme's Vital Statistics * a curve is given showing the number alive at each age out of 100,000 females born alive. From this a period was selected, corresponding in range with Table I. It was then possible to get the proportion of females alive in each quinquennium, and knowing from Table I the incidence during these periods, a percentage incidence for each quinquennium could be obtained on the numbers alive. As 234 cases might be an insufficient number, a similar set of figures was worked out, taking the 1971 cases of uterine cancer dealt with in a previous number of these Archives.* The results are set down below :—

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* Vital Statistics. Newsholme. Edition 1889.

TABLE II.

Showing the Proportional Incidence in the various Quinquennia, given as a percentage on the Survivors of 100,000 *Females, using* 234 *and* 1971 *cases respectively.*

Age periods	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79
Averages of the 234 cases.	·001	·006	·035	·059	·073	·071	·078	·051	·032	·009	·013	·018
Averages of the 1971 cases.	·011	·106	·221	·441	·598	·656	·608	·404	·354	·200	·096	·076

From this table it is seen that the incidence of cancer of the cervix is more common during the 50–54 quinquennium according to one set of figures—and in the 45–49 quinquennium if the larger number of cases be reckoned—when equal numbers of women at different ages are taken.

Since fewer women are alive at the later periods, the numbers given above are of course not representative for the total female population. They express indeed an individual's true chance of getting this form of cancer as she passes through life. This is graphically charted (cf. Plate); the curve is drawn from the 234 cases.

The rise in old age is probably not accurate; the number of cases then was too small. It is not shown in the larger series (Table II), where more cases are available.

Onset in relation to Menopause.—In by far the greater number this was calculated from direct information; a few times, where no information was given, it was reckoned as before or after a menopause estimated at 45·5 years. The disease in 122 cases—54·70 per cent.—began before, in 89 after, and in 12 more or less synchronously with this phenomenon.

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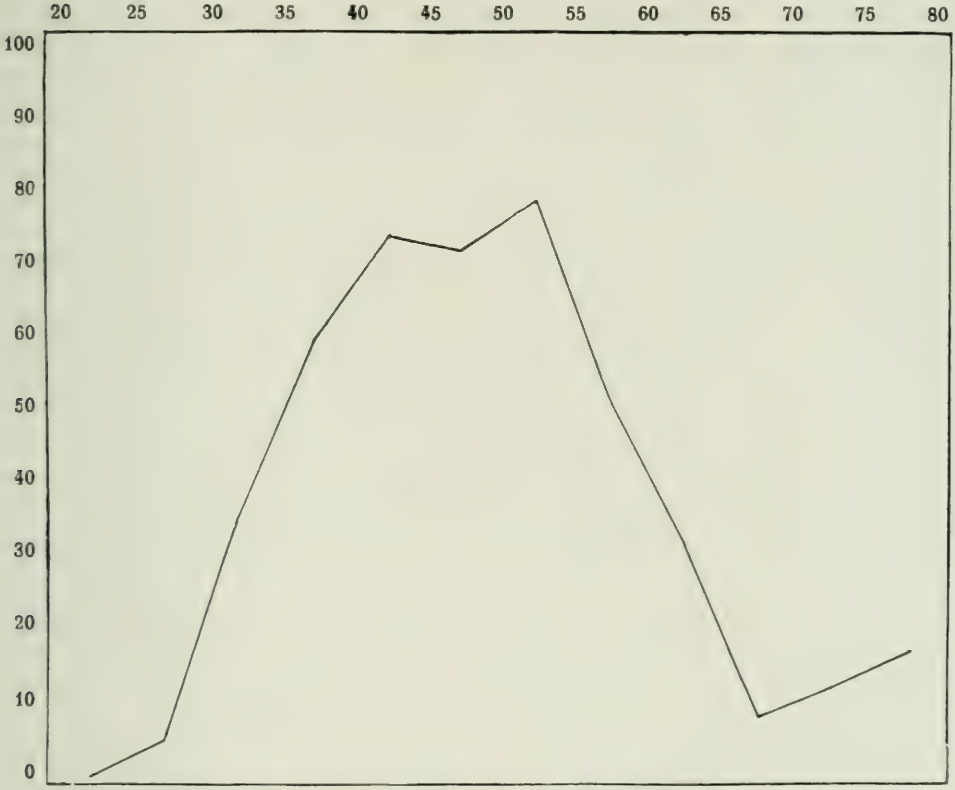
* "Cancer Ages." W. S. Lazarus-Barlow. These Archives, 1905.

Showing Graphically the Incidence, corrected for the Number surviving at each Age-Period. This expresses the Liability to Cancer of the Cervix at Different Ages.



The ordinate gives the number of cases: the abscissa the age.

It was stated, in 184 cases, that menstruation was regular. Only in 14 had irregularity been noted.

TABLE III.

Age at onset	10	11	12	13	14	15	16	17	18	19
Number of cases	4	15	13	33	41	43	18	11	3	1

The above table gives the number of females who began to menstruate at the stated ages and who subsequently developed cancer of the cervix.

Duration of Sexual Life.—By subtracting menstrual onset from climacteric onset, the duration of sexual life is got.

TABLE IV.

Age of onset of menstruation.	11	12	13	14	15	16	17	18
Number of cases analysed.	5	4	11	14	18	5	7	2
Average age for menopause.	47·4	48·0	49·5	49·5	47·1	45·0	47·5	42·0
Mean sexual life in years.	36·4	36·0	36·5	35·5	32·1	29·0	30·5	24·0

This table supports the view (confirmed by Andriezen and Leitch) that sexual life is shorter among those who begin to menstruate late.

TABLE V.

Showing the relative onset of disease in "Sexual" and Somatic life.

Age at which menses began.	11	12	13	14	15	16	17	18
Number of cases analysed.	15	16	29	42	41	20	10	3
Somatic age of onset	46	47·3	44·9	46·3	45·4	46·1	49·7	59·3
"Sexual" age of onset	35	35·3	31·9	32·3	30·4	30·1	32·7	41·3

The lowest set of figures in the above table—the "sexual" age at onset—was obtained by subtracting the age when menstruation began from that at which disease first showed itself. Where the figures are large enough to give approximately accurate results, this age is seen to be remarkably constant; and, indeed, it would appear that the age-incidence for carcinoma of the cervix falls more naturally into the sexual than into the somatic age. Further, Table II shows that the disease claims its maximum number of victims towards the end of sexual life, and, as has been shown, it selects in 54·7 per cent. women who have not reached the menopause. It was found that 46·15 years represented the average age when the first symptoms began.

Cessation of Menses.—In 82 cases the time of menstrual cessation had been noted. This gives a mean age of 47·7 years.

Duration of the Disease.—By subtracting the age when symptoms first presented themselves from the age at death, this was obtained. Cases were classified under two headings; those where some operation, slight or great, had been done, and others where none had been performed.

TABLE VI.

—	Total number.	Average duration of life after onset of symptoms.	Longest in the series.	Shortest in the series.
Cases operated on.	25	2·34 years	5 years	1 year
Cases not operated on.	92	1·66 years	6 years	6 months

And further, it should be noted that in the above table no account can be taken of those cases where, after operation, complete recovery has followed.

TABLE VII.

Giving the Average Duration in Years during the various Quinquennial Age-Periods of all cases.

Age	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79
Number of cases	2	9	20	16	16	24	12	10	0	4	1
Average	1·00	1·83	1·71	1·54	1·66	2·10	1·89	1·69	—	1·81	1·00

This shows a gradual increase in the duration of the disease, up to 50–54 years.

Clinical.

All figures set down below can be only roughly approximate, as a result of the personal factor of the several observers, the different stages at which cases were first seen, and other variants.

Pain was present in 131 cases. In 46 this symptom was not pronounced enough to be noted; of these 18 came subsequently to the post-mortem room.

Hæmorrhage, slight or profuse, was present 184 times; in 14 cases—of which 4 were ultimately subjected to an autopsy—it was either absent or so little that it escaped note.

Emaciation was observed 103 times, and was slight or absent in 64 cases.

Micturition was troublesome in 56; there was gastro-intestinal disturbance 40 times, and difficulty with defæcation 26 times.

Pathological.

On 107 occasions a post-mortem examination was obtained, all the findings being subsequently confirmed by the microscope. Of these cases, in only 48, or 44·85 per cent., was any secondary deposit found either in glands or in viscera. These were placed as follows:—

In glands only	27 cases
In viscera only	6 ,,
In both glands and viscera . . .	15 ,,

The number of times any viscus was invaded is given below:—

Liver . .	14 times	Heart . .	2 times
Spleen . .	7 ,,	Pleura . .	1 time
Lungs . .	5 ,,	Scalp . .	1 ,,
Ovary . .	5 ,,	Spine . .	1 ,,
Peritoneum .	4 ,,	Colon . .	1 ,,
Kidney . .	3 ,,	Thoracic duct .	1 ,,
Suprarenal .	2 ,,	Stomach . .	1 ,,

Most surprising in the above list is the frequent splenic deposit. The records of these Laboratories during the six years 1903–1908 give altogether an account of 16 cases of malignant growth in this organ, all secondary. Carcinoma of the cervix accounts for 8 cases, sarcomas in general for 5, cancer of the breast for 2, and papilliferous ovarian cystadenoma for 1. When it is remembered, as shown above, that in carcinoma of the cervix visceral metastases are of rare occurrence, this frequency is the more remarkable.

Particulars of the distribution of metastases to lymphatic glands show that the lumbar group, which is out of reach of the surgeon, most often becomes involved. Details are shown below :—

Thoracic glands	8 cases
Lumbar glands	28 ,,
Iliac glands	6 ,,
Inguinal glands	6 ,,
Sacral glands	1 case
"Retroperitoneal" glands . . .	1 ,,

In 132 instances ulceration of the growth was found, while in 21 the information given suggested the absence of this condition. These facts were obtained from statements made at the first examination of the patient.

The bladder was involved 19 times without any perforation of its wall. On 48 occasions a vesico-vaginal fistula had formed, while an opening had been established between vagina and rectum 6 times, and between vagina and bladder and rectum 15 times.

The kidney was often the site of pathological change, as the following shows :—

TABLE VIII.

	Hydronephrosis	Pyonephrosis.	"Fibrotic."	"White."	"Surgical."
Right Kidney	19	5	3	1	—
Left Kidney	10	5	6	2	1
Both Kidneys	36	3	4	—	2

The notes refer often to twitchings, headache, and vomiting, suggesting that uræmic symptoms were not infrequently the direct cause of death.

Histology.

In the following tables a classification of the microscopical findings is given :—

TABLE IX.

Squamous Cell Carcinoma.

All layers.	Malpighian and Prickle.	Malpighian alone.	Prickle alone.	Not classified.
9	3	8	6	56

TABLE X.

Columnar Cell Carcinoma.

No metastases.	Glandular metastases.	Visceral metastases.	Glandular and Visceral metastases.	Becoming transitional and no metastases.
4	1	0	1	2

TABLE XI.

Various

Doubtful.	Endothelioma.	Spheroidal Cell Carcinoma.	Double Primary Carcinoma.
3	9	4	1

SUMMARY.

In comparing the foregoing figures with those of Andriezen and Leitch, it is found that they are very much alike. Below the main findings are set side by side :—

	(L. and A.).	(H.M.C.).
Unmarried women . . .	4·59 per cent.	5·5 per cent.
Sterile married women . .	9·0 ,,	6·4 ..
Mean age of onset . . .	44·63 years	46·15 years
Commencing before menopause	51·0 per cent.	54·7 per cent.

	(L. and A.).	(H.M.C.)
Duration of disease (in cases not operated upon) . . .	1·74 years	1·66 years
Cases where there was any secondary deposit . . .	45 per cent.	44·85 per cent.
Secondary deposits :—		
Liver	13·5 ,,	13·1 ,,
Lung	6·0 ,,	4·7 ,,
Kidney	2·6 ,,	2·7 ,,
Heart	1·0 ,,	1·9 ,,
Spleen	1·0 ,,	6·5 ,,
Histology :—		
Squamous-cell carcinoma .	72·5 ,,	79·1 ,,
Columnar-cell carcinoma .	8·1 ,,	7·8 ,,
Spheroidal-cell carcinoma .	4·0 ,,	3·9 ,,
Endothelioma . . .	15·4 ,,	8·7 ,,

The frequency of splenic metastasis gives the most discordant result. During the years analysed in this paper, such a metastasis has been comparatively common, and it will be interesting to see whether future examinations confirm this finding.

It is suggested that the onset is related to the "sexual age" of the individual, and happens most often about the thirty-first year after the beginning of menstruation (Table V).

That kidney disease frequently complicates carcinoma cervicis is well known and to be expected from anatomical considerations; this contention is supported in Table VIII.

Finally, from facts shown in Table II it appears that the liability of any individual woman to become the subject of this disease increases up to about fifty years of age, and becomes almost as unlikely among the old as in young adults. Or it may be stated that it is most likely to occur when the uterus is approaching its Physiological death. It would indeed seem to be the disease not of an ageing individual, but of an ageing uterus.

MALIGNANT DISEASE OF THE THYROID GLAND.

By HELEN CHAMBERS.

The details for the present paper have been obtained from the cases of primary malignant disease of the thyroid gland recorded in the registers of the Royal Free and Middlesex Hospitals. For permission to use the former I am indebted to the authorities of the Royal Free Hospital. Some of the cases have already been published by Mr. James Berry in his book on Diseases of the Thyroid Gland, 1901, and also in a paper entitled "An Analysis of 274 additional cases of removal of growth by operation," in the Proceedings of the Royal Society of Medicine in 1907. It has, however, been thought worth while to collect all the available material illustrating malignant disease in this situation and study the relation of the pathological and clinical aspects.

To Mr. Berry I am much indebted for permission to use the material and clinical notes of his private cases, in addition to those which were under him in the Royal Free Hospital.

Twenty-three cases have been collected, 15 cases of infiltrating malignant disease of the thyroid, and 8 of thyroid tumours of doubtful malignancy. The earliest is from the records of 1899, the last was operated on in February 1909, a period of ten years.

It is impossible from the statistics collected to gain any true idea of the prevalence of malignant disease of the thyroid as compared with that of innocent goitre. Operative treatment is only undertaken in a small number of the cases in which malignancy is suspected, and only those cases are considered here in which it has been possible to study the histological nature of the growth. An examination of the records of the Royal Free Hospital for the period 1900–1908 inclusive shows that during this time 10 cases of malignant disease of the thyroid were treated as compared with 259 cases of innocent goitre. Many of the specimens of goitre referred to in this paper are now preserved in the museum of the Royal Free Hospital—in a few cases it has only been possible to find microscopic sections. All cases in which neither specimen nor sections are available are excluded.

Sarcoma of the Thyroid Gland.

The cases of sarcoma form a group which is closely comparable with sarcomatous tumours in other organs in that they are rapidly-growing tumours—attaining an enormous size—infiltrating surrounding structures and causing death in a comparatively short space of time. Eight cases have been collected; 6 were in women, 2 in men. With the exception of one case who was aged 25, all the patients' ages range between 46 and 55.

Duration.—The shortest duration of the disease was four months, and in this time the growth had formed an enormous mass extending from the chin to the clavicles. The longest duration of the disease was nineteen months from the commencement of symptoms; there was in this case a history of a swelling in the neck for two or three years previous to the onset of symptoms.

Clinical Observations and Symptoms.—In all the cases the growth formed an irregular hard mass in the position of the thyroid gland. In 3 cases it was bilateral. It involved chiefly the left lobe in 3, and in 2 cases the right lobe.

The most marked symptoms, with the exception of one case, were dyspnœa and dysphagia, due to pressure of the growth on the trachea and œsophagus. In Case 8 extensive ulceration of the skin occurred and dyspnœa was never marked.

Pain in the neck and shoulder and tenderness of the tumour are only recorded in one case.

Symptoms due to pressure on nerves in the neck are recorded in four of the cases. Three of these had paralysis of one or both recurrent laryngeal nerves—one case had paralysis of both sympathetic nerves.

The growth in an early stage is fixed to the larynx and trachea, but for some time moves on swallowing.

Treatment and Results.—Operation was undertaken in 5 cases, and an attempt made to remove the growth. In 3 of the cases tracheotomy was done for dyspnœa.

Seven of the patients have died. The remaining one was discharged convalescent in July 1908, and has not been traced. Of the cases which died, in one, death occurred several days after an operation for extirpation of the growth, two died soon after tracheotomy became necessary for dyspnœa, one died after severe hæmorrhage from the common carotid artery, one from septic absorption due to extensive ulceration of the skin, one died suddenly of asphyxia, and one case died with local recurrence, dyspnœa, and general emaciation.

Post-mortem Records are found in 4 cases—in one the examination was limited to the neck. In 2 cases the growth formed a large mass, filling up the front of the neck and extending from the chin to the clavicles. In Case No. 2 it formed a mass the size of a clenched fist on either side of the trachea.

In all cases extensive infiltration of the soft tissues had occurred. The large vessels of the neck tended to be embedded in growth, and were not simply pushed aside as they are in cases of large innocent goitres.

The trachea in all the cases was surrounded and compressed. Penetration of the tracheal wall by growth had occurred in one case only.

Infiltration of the wall of the pharynx and œsophagus is recorded in one case, and of the internal jugular vein in Case No. 8.

The clavicles and sternum were involved by direct extension in two cases.

Lymphatic Glands.—In only one case is there any record of the lymphatic glands being found infiltrated at the post-mortem examination, and in one case the glands were found enlarged at the time of operation.

Metastasis.—In 3 cases in which post-mortem examinations were made one only had metastasis. In this case numerous small nodules of growth were scattered over the surfaces of both lungs, the largest being half an inch in diameter. No other metastatic growths were present.

Characters of the Tumour.—The cut surface of the growth was white, opaque, and almost homogeneous in all the cases. Two cases showed evidence of degenerative changes; in one secondary septic changes had supervened; in the other, the largest tumour, the tissue in the centre of the growth was becoming greyish, soft, and semi-translucent.

Histology.—Four of the cases are spindle-celled sarcomata, 3 are round-celled sarcomata, and one is a mixed tumour composed of round and spindle cells and contains many large giant cells. They are all richly cellular growths with little intervening supporting tissue, and are similar in structure to sarcomata occurring in other organs.

The cases of malignant disease of the thyroid which do not fall into the group of sarcomata just considered are difficult to classify. The extremely slow course of the disease in some cases gives it characters very different from those of malignant disease in other organs, and makes the distinction between an innocent and malignant tumour in some cases very difficult to define.

Tumours occur which in their histological structure are indistinguishable from certain innocent adenomata, and yet the growth extends beyond the capsule of the gland, infiltrates surrounding structures, and causes metastasis. On the other hand there are some apparently innocent growths, in that they are circumscribed, do not extend beyond the capsule of the gland or infiltrate the tissues around, which have a histological structure usually considered as belonging to growths of a definite malignant and infiltrating type. The diagnosis between an innocent and malignant growth can hence in many cases only be decided by the subsequent history of the case, and is often extremely uncertain even when the case has been operated on and the local relations of the tumour determined. In some of the cases in this series a growth which by its subsequent course and infiltrating characters is certainly malignant at the time of operation was fairly easily removed, was circumscribed and had not infiltrated beyond the capsule of the gland. On the other hand a growth as in Case No. 10, apparently definitely malignant at the time of operation in that it had infiltrated the surrounding structures and the trachea, and microscopically had infiltrated a large vessel, is eighteen months later little, if at all, advanced; the patient is in excellent health, and has only a small local recurrence which forms a smooth, rounded, non-infiltrating spherical mass one inch in diameter.

In this paper the cases will be considered in two groups:—

(1) Infiltrating malignant disease of the thyroid; and
(2) Tumours of doubtful malignancy.

Infiltrating malignant disease of the thyroid comprises two groups of cases—(1) the Sarcomata which have already been considered, and (2) the Carcinomata.

Carcinoma of the Thyroid.

Seven cases are included under this heading—5 in women and 2 in men. The patients' ages vary from 43 to 61 years.

Duration.—The disease in many cases has a very protracted course. In one case the duration is 17 years, in one 14 years, in one 11 years, and in two others 4 and 5 years respectively.

In discussing the question of the duration of the disease the possibility of a malignant growth having supervened on an old goitre has to be considered, for in this case the commencement of the malignant growth cannot be dated from the time when a swelling in the neck was first noticed. In none of the 7 cases in this series does the macroscopic appearance of the growth give any reason for supposing that this has occurred, and taking into consideration the extremely slow rate of growth in some of the cases which have been under observation, it seems probable that in many of these cases the condition is rather one of a continuous slow growth of a malignant tumour than a growth supervening on an innocent goitre.

Case No. 10 illustrates this point. The patient, a man æt. 61, had noticed a swelling in his neck for three months giving rise to some pain and dyspnœa. An operation was performed by Mr. Berry in June 1907, on account of suspected malignancy, and an irregular lobulated mass involving the right lobe of the gland was removed. It was adherent to the surrounding structures and was apparently infiltrating the trachea over an area the size of a shilling, and microscopically showed a carcinomatous growth invading a large vessel. The patient is now, eighteen months later, in excellent health. A small recurrent nodule was removed in March 1909. It was round, perfectly circumscribed, smooth, and non-infiltrating, but had identical histological characters with those of the primary growth. No other growth was seen at the second operation.

Clinical Observations and Symptoms.—In 6 of the cases the tumour formed a hard swelling in the position of the thyroid gland, in one case it was largely substernal. It was bilateral in 4 cases, involved the right lobe in 2 cases, and the left lobe in one.

The prominent symptoms, as in the sarcomata, were dyspnœa and dysphagia, due to pressure of the growth on the trachea and œsophagus.

One or other vocal cord was paralysed in 3 cases. Pain is not a marked symptom until the later stages of the disease. It is noted in 4 cases.

Treatment and Results.—All the 7 cases have been operated upon, and an attempt made to remove the growth; 4 cases died soon after the operation. Of the remaining 3 cases one has died two years later with local recurrence and growth infiltrating the sternum; one lived for fifteen months after the operation, and was for many months in good health—eventually, however, there was local recurrence; Case No. 10 is now alive and in excellent health. A recurrent nodule was removed in March 1909.

Characters of the Tumour.—The outer surface of the tumour in most cases is nodular, in a few it is smooth. The cut surface shows solid yellowish white or grey tissue differing completely from the appearance of normal thyroid tissue and from the commoner colloid adenomata in its solid opaque characters.

Degeneration seems to be an unusual feature, and none of these cases shows any tendency to softening, cyst formation, or to hæmorrhage into the growth. In two of the cases the centre of the mass contained an irregular area of yellow fibrous tissue.

Post-mortem Records are found in 3 cases; in one of these the examination was limited to the neck. The muscles in all were infiltrated with growth. The trachea was invaded in one case, and a small pedunculated mass projected from its inner surface. Extension of the growth to the manubrium had occurred in one case, and the bone was extensively softened.

Metastases.—One case showed numerous small metastases in both lungs, but none elsewhere.

In Case No. 12, although the primary growth was large, and extensive infiltration of the surrounding structures had occurred, no metastases were found.

Lymphatic Glands.—There is no record of infiltration or enlargement of the lymphatic glands either at the time of operation or post mortem.

HISTOLOGY.

It is impossible to describe the so-called carcinomata of the thyroid as a single group. As will appear from the following descriptions almost each case has its own individual histological character.

Case 9.—The growth has the structure of a columnar carcinoma. It contains many glandular spaces varying in size and shape, some being round, oval, or irregular, and others elongated into long tubular channels. They are lined, in many places, by a single layer of columnar epithelium. In other places the cells have undergone proliferation, and form a layer several cells in thickness lining the alveoli and tending to subdivide the central space into smaller cavities. The glandular character is everywhere marked, and only very few of the alveoli are filled with cells. Many of the spaces contain colloid-like material.

The interstitial tissue in places is scanty, in other parts it forms wide strands of fibrous tissue separating the alveoli. The structure of the whole growth is very similar to that of a columnar-celled carcinoma of the rectum.

A section across the internal jugular vein shows it completely blocked with growth having a similar structure.

Case 10 has a histological structure shown in Plate I, Fig. 1, and is very similar to Case 9. Many of the alveoli are completely filled with cells. Others have a very distinct lining of columnar epithelium, and the growth on the whole has a more cellular character.

Case 11.—A tumour closely similar in histological structure to the thyroid gland in an early fœtal condition (Plate I, Fig. 2). It consists of two types of tissue: (1) Containing glandular spaces of varying size, some extremely small, others large and cystic, either round, irregular, or tubular in shape, and lined by a single layer of cubical epithelium, which occasionally shows columnar characters; and (2) An intervening tissue composed of solid masses of cells in some places arranged in groups, in others diffusely scattered with no definite arrangement, and in close relation with the interstitial tissue. The cells have similar staining characters to those lining the alveolar spaces, and have single, deeply staining nuclei and little protoplasm. Some parts of the growth consist almost entirely of the first type, in other parts the second type predominates, and the growth here would be entirely solid but for the large vascular channels passing through it.

The interstitial tissue is scanty and contains many very large blood spaces and lymph channels, which in places break up the tissue and give it a spongy nævoid structure.

Case 12.—A growth having a histological structure similar to Case 11, but on the whole less vascular.

Case 13.—Histologically a growth similar to Cases 11 and 12. The alveolar arrangement is more marked, and the gland-spaces are better formed and filled with colloid. There is less intervening solid tissue.

A section through a metastatic nodule in the lungs has a similar structure. It contains many gland-spaces lined by single layers of low columnar epithelium and filled with colloid material. There is very little interstitial tissue, and very few of the alveoli are solid.

Cases 14 and 15.—The histological structure is that of a richly cellular growth with a definite alveolar arrangement. The alveoli are large and filled with cells proliferating from the walls. There are no glandular spaces to be found, and the growth has characters like those of a spheroidal-celled carcinoma.

These two cases differ from Cases 11, 12, and 13, in that in the latter, besides a distinct glandular structure, there is an intervening cellular tissue having almost sarcomatous characters.

The carcinomata of the thyroid hence fall into two chief groups :—

(1) Columnar carcinomata :

(*a*) Cases in which the growth retains a marked glandular structure and the epithelium is distinctly columnar in type, as shown in Plate I, Fig. 1.

(*b*) Cases in which the columnar character of the epithelium is lost. The growth is composed of alveolar spaces completely filled with cells, and simulates a spheroidal-celled carcinoma.

(2) A class of malignant tumours having a structure very similar to that of undeveloped thyroid tissue, containing many gland-spaces and an intervening solid cellular tissue with almost sarcomatous characters, shown in Plate I, Fig. 2.

The latter tumours are histologically indistinguishable from some benign fœtal adenomata unless there is evidence of the growth infiltrating the tissue outside the capsule of the thyroid gland.*

Tumours of Doubtful Malignancy.

Eight cases are included under this heading. They are difficult to group, and owing to individual peculiarities have to be considered more or less separately.

Three cases of Endothelioma of the Thyroid.—Cases 16, 17, and 18 have a somewhat similar histological structure, and can be grouped together as endotheliomata. They are all single encapsuled tumours removed from patients whose ages were 55, 66, and 68 years.

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* Many of the growths described in the preceding section as well as in that which follows, and many fœtal adenomata, to which no reference is made here, bear a striking histological resemblance to mouse cancer. (W. S. L.-B.)

They are rounded, smooth. non-infiltrating growths, indistinguishable clinically from innocent adenomata, and have been removed by the operation of resection-enucleation.

Case 16.—A tumour weighing 10 oz. and measuring 10, 9, and 4 cms. in vertical, transverse, and antero-posterior diameters. It was one-third substernal, and is somewhat flattened, with a shallow transverse groove across it, corresponding to the line of pressure of the sternum. The cut surface is mottled and contains opaque white areas, intermixed with reddish-brown spongy-nævoid tissue. In the centre there is a narrow irregular mass of fibrous tissue from which prolongations extend into the surrounding growth.

A study of the microscopic sections, Plate II, Figs. 3 and 4, shows a very varied histological appearance in different parts of the tumour.

In the centre the structure is similar to that of an angiosarcoma. The growth here consists of a collection of thick-walled vascular tubes embedded in clear, almost structureless interstitial tissue. Each tube contains a central space lined with flattened endothelium and filled with red blood corpuscles. The wall is formed by a mass of closely packed, deeply staining cells, and is separated from the endothelium lining the central cavity by a thin layer of hyaline material. The tubes are cut in all directions, and are round, oval, or irregular in cross-section (Plate II, Fig. 3).

Near the surface of the tumour, Plate II, Fig. 4, all trace of tubular structure is lost. The growth is richly cellular, with little intervening tissue, and in places only a slight alveolar arrangement is retained by narrow capillary vessels passing amongst the cells. It is here much less vascular. In another part the structure consists of narrow capillary channels running in all directions and embedded in a large quantity of hyaline interstitial tissue. They are lined by endothelial cells which are not flattened against the wall, but are large, project into the lumen, and have large, deeply-staining nuclei. In some places these channels contain blood corpuscles, in other places the endothelium completely fills up the spaces.

Case 17 has a histological structure similar to that in parts of Case 16. The centre of the tumour contains a large amount of necrotic material.

Case 18.—Histologically a typical endothelioma. The growth has a marked alveolar arrangement. The cells are grouped in large masses, embedded in interstitial tissue containing much degenerate material. In many of the alveoli and amongst the cells there are two or three blood spaces lined in some parts by flattened endothelium and filled with blood. In other parts there are similar spaces filled with structureless granular material.

Case 19 can possibly be grouped with the last three cases, and has a structure somewhat similar to that of a psammoma of the brain (Plate III, Fig. 5).

It is an oval solid tumour 1½ in. in diameter removed from the right lobe of the thyroid gland. Its outer surface is rounded and smooth.

The cut surface is white, opaque, and uniformly calcified throughout.

A section for microscopic examination could only be prepared after decalcification in 5% nitric acid.

The histological structure consists of many closely set, irregular gland-like spaces lined with cubical epithelium.

The spaces are filled with calcified exudation laid down in concentric layers, giving it a stratified appearance. A similar exudation is present in the interstitial tissue. The thyroid gland tissue forming the capsule is normal.

Two cases of growth supervening in an innocent Adenoma.—*Cases* 20 and 21 can be grouped together as cases in which a growth has supervened on an innocent adenoma. They are the only cases of this kind which I have been able to find.

Case 20 is an adenoma the size of an orange, removed by enucleation from a patient aged 60 on account of dyspnœa. Clinically it was an innocent tumour.

The outer surface is smooth, the inner surface is covered with ragged pieces of degenerating adenoma tissue. The wall is thick, fibrous, and calcified, and on cutting into it from the inner aspect of the cyst there is at one place a mass of tissue which is white, opaque, and soft. The section has been taken through this place, and hence does not contain any tissue of the thyroid gland except a thinned-out layer on the extreme outer surface of the cyst.

Plate III, Fig. 6, shows the structure near the interior of the cyst, and shows two distinct types of growth, one having the structure of the common type of colloid adenomata, and the other a papillomatous growth staining much more deeply and consisting of strands of connective tissue covered with a single layer of low columnar epithelium.

In this case there can be little doubt that a growth of a different type has developed from the interior of an innocent cystic adenoma.

Case 21 is that of a large tumour weighing 35 oz. removed from the right lobe of the thyroid gland in a female aged 79. There was a history of rapid enlargement for three months.

The tumour was removed fairly easily, and there was no evidence of infiltration of the tissue around the thyroid at the time of operation.

The growth has a slightly nodular surface, is a soft solid, and is uniformly reddish-white in colour. At the lower part there is a colloid adenoma 2 in. in diameter which contains calcareous material.

The microscopic structure is shown in Plate IV, Fig. 7.

It has a marked papillomatous character, and consists of strands of fibrous tissue covered by a single layer of columnar epithelium.

From the rapid growth we should expect this to be a malignant tumour. It had, however, attained an enormous size without infiltrating surrounding tissues, and six months after the operation the patient was in good health.

Two cases of recurrent Adenomata.—The next two cases of recurrent adenomata are discussed here because they may perhaps be considered as on the borderland of malignant growths.

Case 22 is that of a man aged 57, who in the course of 5 years had 5 operations for the removal of encapsuled tumours of the thyroid gland. At these operations the growths removed weighed 32, 8½, 4, and 2 oz. respectively. The last record, in 1906, states that his general health is good, but he has a further recurrence.

The tumours were always rounded, encapsuled, and non-infiltrating. The cut surface of the tissue is solid, white, and soft, with some areas of hæmorrhage.

They all had a similar histological structure (shown in Plate IV, Fig. 8), and consisted of a richly cellular tissue having a somewhat papillomatous character, with delicate strands of connective tissue covered with a single layer of epithelium. The epithelium is peculiar, and consists of flattened polygonal cells rather like pavement epithelium cells with single nuclei and a large amount of protoplasm which is often granular and contains colloid-like material. The papillary processes are in close apposition with each other, and there is no colloid secretion formed in the spaces. The whole growth is very vascular, and in many places there is extravasation of blood.

In *Case* 23 the patient was aged 25, and had in the course of 8 years five operations for removal of adenomatous growths of the thyroid. In February 1907, when the last record of the case was made, the growth had recurred and was about 2 in. in diameter. The patient was otherwise quite well.

The tumours removed were all encapsuled rounded masses easily enucleated from the gland tissue. They are soft, and consist of opaque white tissue containing no colloid.

Microscopically they are richly cellular tumours containing many tubular gland spaces lined with columnar epithelium and an intervening tissue with only slight glandular characters.

The interstitial tissue is delicate and scanty.

CONCLUSIONS.

1. The diagnosis between an innocent and malignant tumour of the thyroid is often extremely difficult to make.

2. Only those cases should be considered as malignant in which the growth ultimately extends beyond the capsule of the gland and infiltrates the surrounding tissues.

3. Without evidence of infiltration many tumours of the thyroid cannot from their histological structure alone be diagnosed as malignant unless they belong to the group of sarcomata.

4. Carcinoma of the thyroid often pursues a very protracted course, and in all cases the prognosis is extremely bad.

5. There exist certain large non-infiltrating tumours having a papillomatous structure which do not tend to infiltrate even when the tumour reaches a large size, and in which treatment by operation offers a satisfactory result.

6. Comparatively few malignant or semi-malignant growths can be demonstrated to have arisen from pre-existing adenomata.

Plate I.

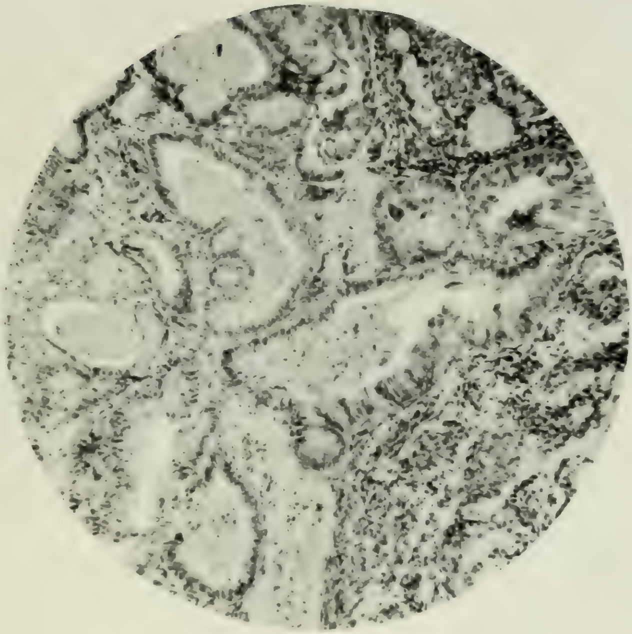

Fig. 1.

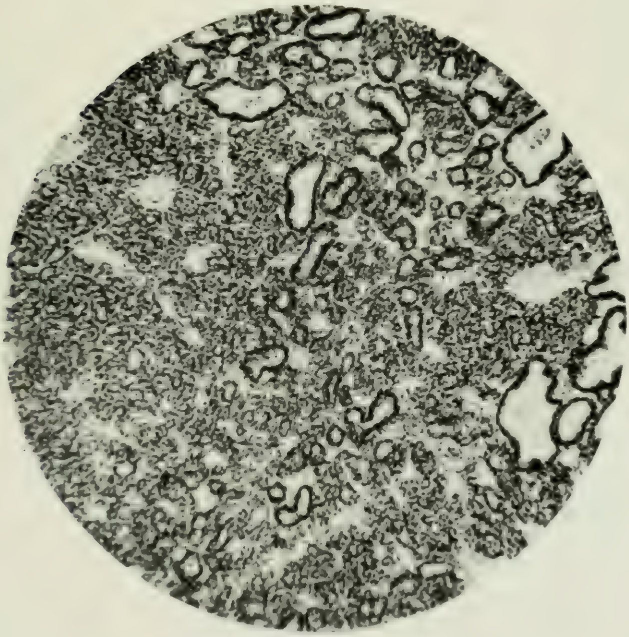

Fig. 2.

Plate II

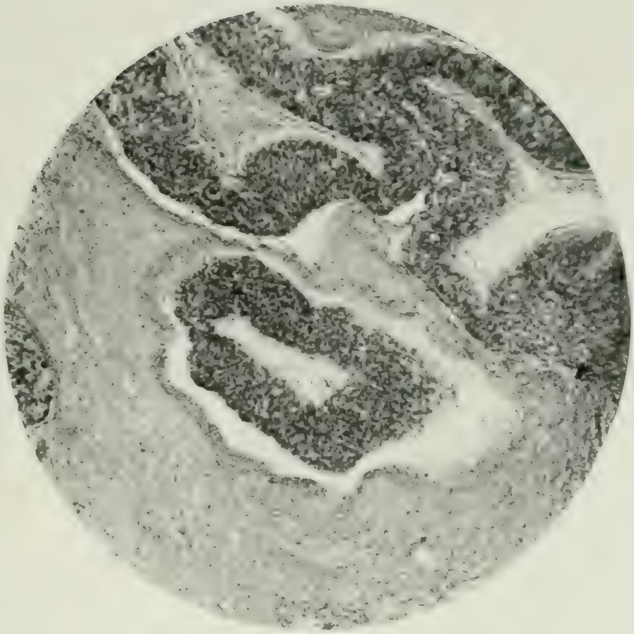

Fig. 3.

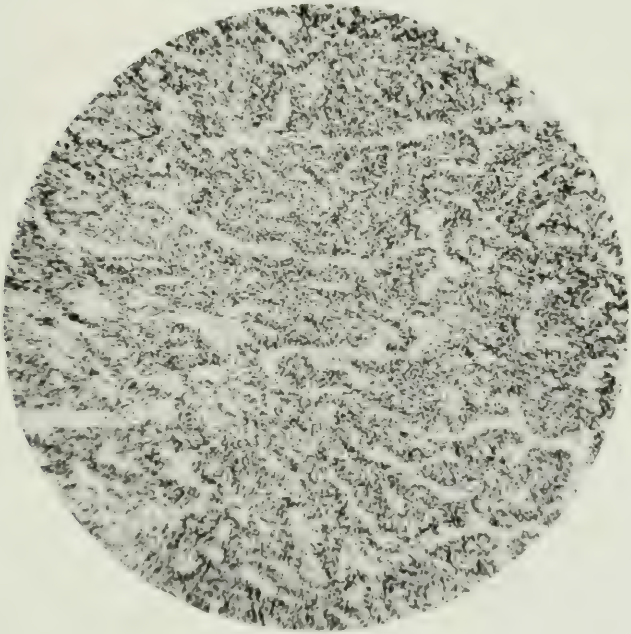

Fig. 4.

Plate III.

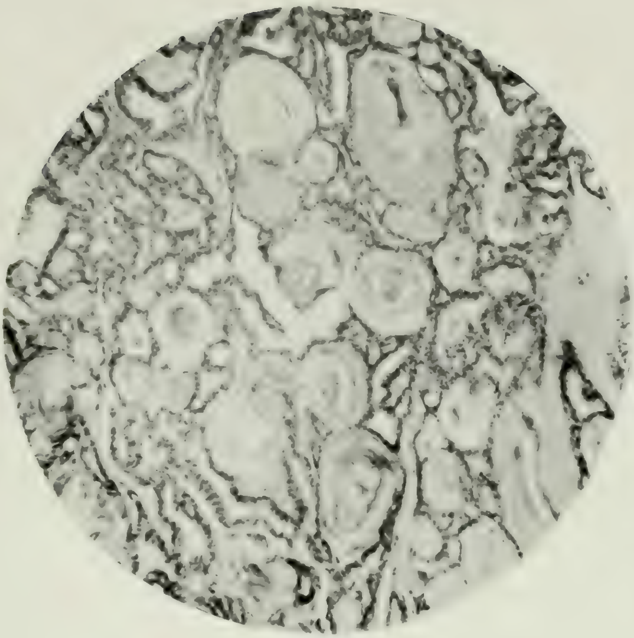

Fig. 5.

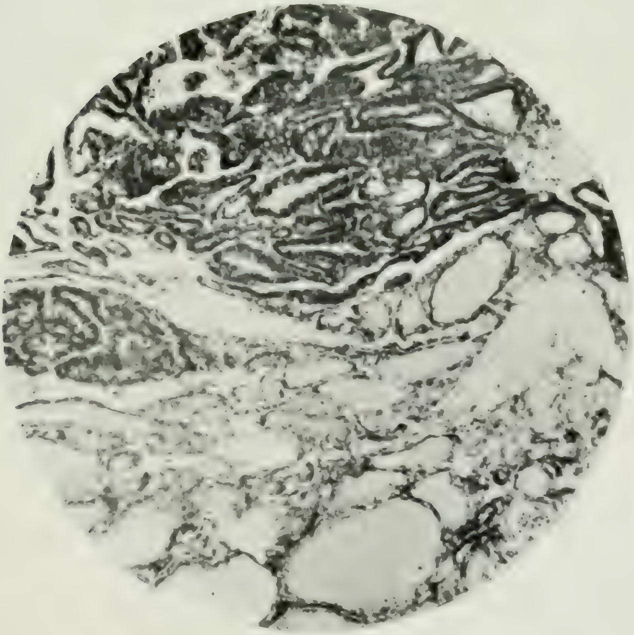

Fig. 6.

Plate IV.

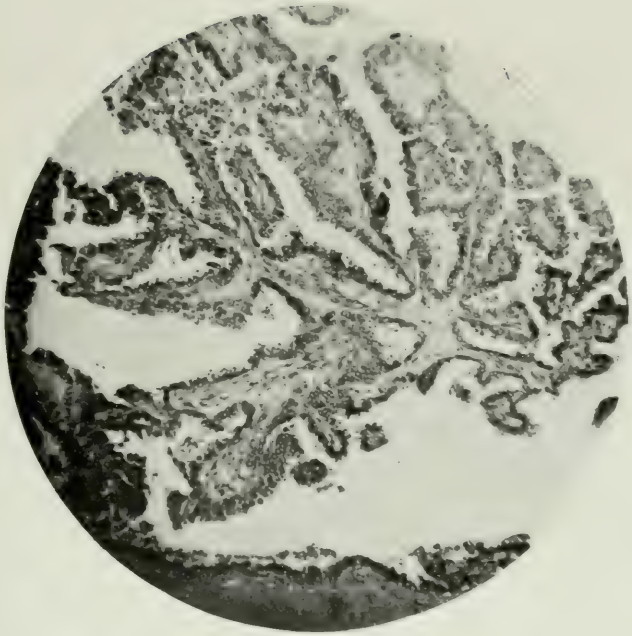

Fig. 7.

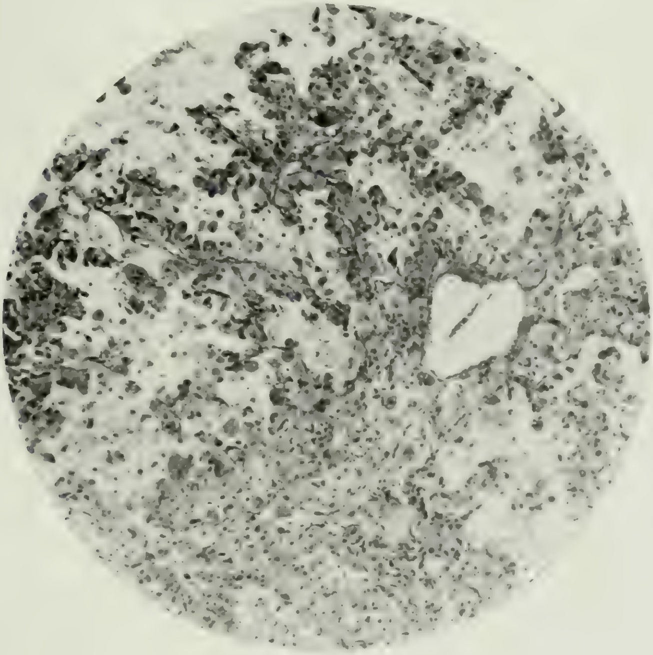

Fig. 8.

SYNOPSES OF 23 CASES OF MALIGNANT DISEASE OF THE THYROID GLAND.

No.	Reference.	Age and Sex.	History.	Local Condition on Admission.	General Health.	Pressure Effects.	Operation.	Nature of the Growth.	After History.	Remarks.
1	C. K. R. F. H. Mr. Berry.	25 M.	4 months' enlargement of neck.	There is a hard swelling in front of and to the left of the trachea 4 inches in diameter. It is fixed to the spine and does not move on swallowing.	Pale, thin.	Dyspnœa. Dysphagia, could swallow liquids only. Both vocal cords paralysed.	Tracheotomy, 1 month before death.	Spindle-celled sarcoma.	Death, Aug. 1899, from severe hæmorrhage from the carotid artery.	Specimen, R. F. H. Museum, No. 54, Series XXII. *Post-mortem examination.* There is a large growth extending from the chin to the clavicles and apparently originating in the left lobe of the thyroid gland. It is adherent to the left clavicle and first rib. The pharynx and œsophagus are much infiltrated with growth. The trachea is displaced to the right, and the left carotid artery is completely surrounded. The cut surface of the growth is white. It is becoming degenerated and softened in the centre. No metastases.
2	F. M. R. F. H. Mr. Berry.	50 F.	14 months' enlargement of neck.	There is a bilateral hard swelling which moves with the trachea and is tender on pressure.	Well nourished.	Attacks of dyspnœa. Dysphagia. Pain in the neck and shoulder Vocal cords not seen.	Feb. 1900. Operation for extirpation of the growth by Mr. Barrow. July 1900. Removal of a portion of the growth in front of the trachea. Tracheotomy by Mr. Berry.	Spindle-celled sarcoma.	Death, July 1900.	Specimen, R. F. H. Museum, No. 55, Series XXII. *Post-mortem examination.* There is a mass the size of a clenched fist on either side of and adherent to the trachea, also to the clavicles and sternum. The muscles are infiltrated with growth. The trachea is surrounded and compressed. No metastases.
3	J. S. R. F. H. Mr. Berry.	49 M.	2 to 3 years' enlargement of neck. 4 months' difficulty in breathing and swallowing.	There is a hard nodular swelling of the left lobe of the thyroid measuring 3 inches by 3½ inches. It is fixed to the larynx and trachea, but moves on swallowing.	Emaciated. Looks ill and tremulous.	Trachea displaced to the right. Dyspnœa. Dysphagia. Left vocal cord paralysed.	Sept. 1902. Left lobe extirpated.	Spindle-celled sarcoma.	Sept. 1903. Readmitted for recurrent growth on the left side the size of a small egg. No further operation. Death, Dec. 1903.	Specimen, R. F. H. Museum, No. 55 B, Series XXII. It is a hard, irregular white mass the size of a small orange. At the time of the operation the growth was adherent to the carotid sheath and to the trachea and œsophagus. The left carotid artery and recurrent laryngeal nerve were removed with the tumour. No post-mortem examination.

SYNOPSES OF 23 CASES OF MALIGNANT DISEASE OF THE THYROID GLAND (*cont.*)

No.	Reference.	Age and Sex.	History.	Local Condition on Admission.	General Health.	Pressure Effects.	Operation.	Nature of the Growth.	After History.	Remarks.
4	S. R. M. H. Mr. Pearce-Gould.	55 F.	Swelling in the neck noticed for 1 year.	Hard, ill-defined swelling of the isthmus and right lateral lobe—moves with the trachea.	Well nourished.	Dyspnœa. Vocal cords normal.	1904. Tracheotomy.	Spindle-celled sarcoma.	Death.	*Post-mortem examination.* A growth involving the right lobe and isthmus. A small polypoid mass projected into the trachea. Larynx normal. The glands on the right side of the neck were infiltrated. Numerous metastatic nodules in the lungs, the largest half an inch in diameter. No metastases elsewhere.
5	M. P. R. F. H. Mr. Legg.	52 F.	Swelling of the neck for 3 months.	Hard, smooth globular swelling in the right lobe. Moves on swallowing. No pain.	No note.	Vocal cords normal. Both sympathetic nerves paralysed.	April 1900. Extirpation of the right lobe.	Round-celled sarcoma.	Death, 12 days after operation.	Specimen. A solid white mass of growth weighing 5½ oz. At the time of operation adherent to the internal jugular vein and to the pharynx. Several enlarged glands seen.
6	Mrs. G. Mr. Berry.	49 F.	19 months ago patient noticed a small lump the size of a walnut.	Densely hard nodular mass on the right side of the neck the size of a small orange.	Healthy.	Dyspnœa.	March 1903. Extirpation of a tumour of the right lobe.	Round-celled sarcoma.	May 1903, death with local recurrence.	Specimen, R. F. H. Museum, No. 55 A, Series XXII. A white, solid, irregular-shaped mass.
7	H. O. M. H. Mr.Murray.	46 F.	Swelling of the neck for 4 months.	Soft, diffuse swelling involving the isthmus and left lobe of the thyroid. Moves on swallowing.	Poorly nourished	Dyspnœa.	June 1908. Extirpation of the left lobe.	Round-celled sarcoma.	July 1908, discharged convalescent.	At the time of operation the growth infiltrated the muscles of the neck.

8	H. F. R. F. H. Mr. Berry.	53 F.	A swelling in the neck the size of a walnut since childhood. 9 months' increase in size.	Hard, irregular swelling the size of an orange, in front of the trachea. Painless. Moves on swallowing.	Well nourished. Anæmic.	Little dyspnœa, only on exertion. Trachea laterally compressed. Vocal cords not paralysed.	None.	Mixed-celled sarcoma. Round, spindle and many giant cells.	1899, death from septic absorption following extensive ulceration of the skin.	Specimen, R. F. H. Museum, No. 53, Series XXII. *Post-mortem examination* limited to the neck. There is a large mass of growth occupying the front of the neck, with three large fungating ulcers of the skin in front. The trachea is surrounded by growth and displaced to the left. There is no growth projecting into it. The left internal jugular vein is infiltrated.
9	M. W. R. F. H. Mr. Berry.	43 F.	Swelling first noticed in the neck 5 years ago. It has slowly increased in size. Some pain.	Oval irregular swelling in front of and to the left of the trachea. Firmly fixed to the trachea and larynx.	Well nourished.	Dyspnœa. Marked stridor. Vocal cords not paralysed.	1890. Extirpation of the right lobe.	Columnar carcinoma.	Death soon after the operation.	Specimen, R. F. H. Museum, No. 24, Series XXII. It consists of the right lobe of the thyroid gland the lower half of which is invaded by a white, solid, homogeneous growth. The upper half is enlarged, but contains no encapsuled masses. No post-mortem examination.
10	C. B. R. F. H. Mr. Berry.	61 M.	3 months' swelling and pain on the right side of the neck. 2 weeks' difficulty in breathing and hoarseness.	Hard, smooth swelling in the right lobe measuring 3½ inches by 2 inches. It moves on swallowing.	Well nourished.	Dyspnœa.	June 1907. Extirpation of the right lobe and isthmus.	Columnar carcinoma.	March 1909. Readmitted. General health excellent. Recurrent nodule removed	The specimen consists of a solid irregular white mass weighing 2½ oz. At the first operation it infiltrated the muscles and the trachea over an area the size of a shilling. At the second operation a round smooth non-infiltrating spherical mass 1 inch in diameter was removed.
11	B. H. R. F. H. Mr. Berry.	48 F.	Swelling in the neck noticed for 4 years. Slow increase in size.	Large hard, smooth swelling in front of and on either side of the trachea. It is fixed to the larynx. Circumference of neck 16½ inches.	Healthy.	Dyspnœa. Stertorous breathing Dysphagia—could swallow liquids only. Vocal cords not paralysed.	March 1906. Resection, enucleation of the left lobe and isthmus.	Carcinoma.	Sept. 1908. Death with local recurrence and secondary growth in the sternum.	Specimen, R. F. H. Museum, No. 83, Series XXII. A solid smooth mass weighing 12½ oz. The cut surface is white with some areas of hæmorrhage. It was not infiltrating the surrounding tissues at the time of operation. No post-mortem examination.

SYNOPSES OF 23 CASES OF MALIGNANT DISEASE OF THE THYROID GLAND (*cont.*)

No.	Reference.	Age and Sex.	History.	Local Condition on Admission.	General Health.	Pressure Effects.	Operation.	Nature of the Growth.	After History.	Remarks.
12	S. B. R. F. H. Mr. Berry.	43 F.	Swelling in the neck noticed for 14 years. Slow increase in size. Some pain for 4 to 5 years.	1902. Prominent hard swelling extending from the hyoid bone to the clavicles and fixed to the larynx. 1903. The swelling has increased in size. 1904. Further increase in size. Circumference of the neck 20¾ inches. No ulceration of the skin.	1904. Emaciated.	1902. Vocal cords not paralysed. Slight dyspnœa. 1903. Right vocal cord paralysed—dyspnœa. 1904. Dyspnœa. Dysphagia—could swallow fluids only.	Jan. 1904. Operation undertaken on account of extremely slow growth of the tumour. Extirpation of the right lobe.	Carcinoma.	Death 50 minutes after the operation.	Specimen, R. F. H. Museum, No. 57 A, Series XXII. An irregular white, hard and solid mass weighing 25 oz. Its cut surface shows a mass of fibrous tissue in the centre, surrounded by yellowish-white growth. *Post-mortem examination.* The muscles and manubrium are infiltrated—the latter is much softened. Trachea and œsophagus are not invaded. No metastases.
13	L. H. R. F. H. Mr. Berry.	58 F.	14 years ago a painless swelling noticed in the neck the size of a walnut. Slow increase in size. 1898. Adenoma enucleated, wt. 4 oz. 1 year later growth recurred and has grown slowly for 2½ years and more rapidly for 6 months. Total duration 17 years.	1902. Large irregular swelling occupying both sides of the neck, and consisting of four globular masses. It moves with the larynx.	Well nourished.	Right vocal cord paralysed. Dyspnœa.	Jan. 1898. Adenoma enucleated, said to be innocent. May 1902. Extirpation of the right lobe. Wt. = 11 oz.	Carcinoma.	Death 2 days after the operation.	*Post-mortem examination.* Muscles infiltrated with growth. Pharynx, trachea, œsophagus, and larynx not infiltrated. Metastases. Small secondary nodules in both lungs—none elsewhere.

14	A. H. R. F. H. Mr. Berry.	60 F.	Indefinite history. A swelling noticed for 1 year. 6 months' dyspnœa and difficulty in swallowing. Pain in the right side of the neck.	Soft tense rounded swelling the size of a tangerine orange on the left side. Tumour chiefly intrathoracic.	Well nourished.	Veins on the right side of the neck much enlarged. Vocal cords not seen.	June, 1902. Partial extirpation of the right lobe. Both lobes enlarged and forming intrathoracic tumours.	Carcinoma.	Death soon after the operation.	Local examination of the wound only. The trachea contained a small pedunculated mass of growth.
15	Mr. L. Mr. Berry.	52 M.	Healthy until 10 years ago, when a lump was noticed in the neck. It gave no trouble for some years. 1 year dyspnœa.	A large hard mass occupying chiefly the left lobe, the size of a clenched fist.	Well nourished.	Dyspnœa. Larynx displaced to the left. Vocal cords not seen.	Oct. 1906. Extirpation of the left lobe.	Carcinoma.	Jan. 1908. Death, with local recurrence. In good health for many months after the operation.	Specimen, R. F. H. Museum, No. 81 B, Series XXII. At the time of operation the growth was found adherent to the pharynx and larynx. There were no enlarged lymphatic glands. The specimen is a solid irregular tumour weighing 5 oz. Its cut surface shows a central mass of fibrous tissue surrounded by rounded masses of solid yellow growth.
16	F. G. R. F. H Mr. Cunning.	55 M.	Swelling in the neck noticed for 2 years 3 months' difficulty in breathing.	Hard, smooth swelling on the right side of the neck and extending to the clavicle.	Well nourished, healthy.	Dyspnœa. Palpitation.	June 1907. Enucleation.	Endothelioma.	June 30th, 1907. Discharged well.	Specimen, R. F. H. Museum, No. 81 A, Series XXII. An encapsuled ovoid tumour one-third substernal. Wt. 10 oz. No infiltration.
17	Mrs. D. Mr. Berry.	68 F.	Tumour of long duration.		Poorly nourished.	Dyspnœa.	Dec. 1906. Substernal adenoma of the right lobe removed.	Endothelioma.	1906. Death from heart failure	Round, smooth encapsuled mass the size of a small orange, and containing soft brown degenerate material. Clinically an innocent tumour.
18	T. F. R. F. H. Mr. Berry.	66 M.	Swelling of the neck for 2-3 months. Several years' dyspnœa.	Hard, smooth lump on the right lobe. Moves on swallowing.	Healthy.	Slight dyspnœa. No dysphagia. Vocal cords normal.	1908. Operation for suspected malignancy. Right lobe extirpated.	Endothelioma.	Discharged well, Jan. 1909.	The tumour is a circumscribed spherical mass in the right lobe 2 inches in diameter. It is non-infiltrating, and is covered by a thin capsule of thyroid gland tissue. The cut surface is reddish-white soil-growth. No enlarged glands in the neck.

SYNOPSES OF 23 CASES OF MALIGNANT DISEASE OF THE THYROID GLAND (*cont.*)

No.	Reference.	Age and Sex.	History.	Local Condition on Admission.	General Health.	Pressure Effects.	Operation.	Nature of the Growth.	After History.	Remarks.
19	W. H. R. F. H. Mr. Berry.	41 M.	Swelling noticed for 1 year. Slowly increasing in size.	Smooth, extremely hard swelling in the right lobe of the thyroid gland.	Healthy.	No dyspnœa. No dysphagia.	Operation for suspected malignancy. 1903. Enucleation.	Calcified endothelioma.	1903. Discharged well.	Specimen, R. F. H. Museum, No. 66 A, Series XXII. An oval solid tumour 1½ inches in length. The cut surface is white, extremely hard, and uniformly calcified throughout.
20	Miss A. Mr. Berry.	79 F.	Swelling on the right side of the neck for some years. 3 months' rapid increase in size.	Right lobe of the thyroid much enlarged and adherent to the larynx.	Fairly healthy, pale.	Right vocal cord paralysed.	July 1908. Extirpation of the right lobe.	Papillomatous tumour arising in an old adenoma.	Quite well at the end of 1908.	Specimen, R. F. H. Museum, No. 57 B, Series XXII. A large mass of growth weighing 35 oz., and covered on the outer surface with fascia. At the lower part there is an old spherical adenoma 2 inches in diameter which is partially calcified. The cut surface of the growth is white and soft, no normal thyroid tissue can be seen. At the time of operation there was no infiltration of the tissues around.
21	Dr. M. Mr. Berry.	60 M.	A swelling of many years' duration.	An encapsuled tumour of the left lobe of the thyroid.	No note.	Dyspnœa.	1900. Enucleation.	Papillomatous growth arising in an old adenoma.	Death from thoracic aneurism.	Specimen, R. F. H. Museum, No. 48, Series XXII. A large cystic adenoma the size of an orange. The wall is tough, fibrous, and partly calcified, and on the inner aspect has many ragged shreds of degenerate adenoma tissue attached to it. At one part there is a solid white opaque mass. On microscopic examination a papillomatous growth from the inner wall of the cyst.

22	W. G. R. F. H. Mr. Berry.	57 M.	1906. Swelling of the neck for 11 years. Repeated operations.	1906. A swelling 2 inches in diameter in the left lobe and 2 other smaller swellings. Glands on the right side of the neck slightly enlarged.	Well nourished.	Dyspnœa. Vocal cords not paralysed.	1902. Adenoma removed from right lobe. Wt. = 32 oz. 1903. Adenoma removed from the right lobe. Wt. 8½ oz. 1904. Operation on the left lobe. 1905. Right-sided tumour removed. Wt. = 4 oz. 1906. Tumour from the left lobe. Wt. = 2 oz.	Recurrent adenomata. ? Papillomatous growth.	1906. Discharged well. Oct. 1906. Good general health. Local recurrence.	Specimen. R. F. H. Museum, No. 76, Series XXII. Part of the right lobe of the thyroid gland containing a large spherical smooth tumour, and weighing 32 oz. The cut surface shows solid mottled growth, largely white and opaque, in parts containing brown, clearer areas. Specimen, R. F. H. Museum, 76 A. A solid tumour 2 inches in diameter. The cut surface is white and soft.
23	L. S. R. F. H. Mr. Berry.	25 F.	Blow on the neck 17 years ago. A swelling appeared afterwards. 5 operations for the removal of adenomata.	1906. Both lobes enlarged by rounded swellings, which move with the trachea. Some pain on the right side. No exophthalmos.	Well nourished.	Dyspnœa. Vocal cords normal.	1898. 2 operations for removal of adenomata. 1900. 3rd operation. 1903. 4th operation, mass removed. Weighed 7 oz. 1906. 5th operation. Wt. of specimen = 2 oz.	Recurrent adenomata.	Feb. 1907. General health good. Local recurrence, and a lump 2 inches in diameter.	Specimen. Round encapsuled tumours—soft, white, and opaque on section. No infiltration.

ON PRIMARY MALIGNANT DISEASE OF THE OVARY.

By BRYDEN GLENDINING.

In the following article a statistical study is made of 41 cases of primary carcinoma of the ovary, of 16 cases of primary sarcoma, and of 50 cases of papilliferous cystadenoma admitted to the Middlesex Hospital during the years 1854–1908.

PRIMARY CARCINOMA OF THE OVARIES.

There are here considered 41 cases of primary carcinoma of the ovary for the period 1854–1908.

Age.—The age is reckoned as that of the patient upon presentation for treatment. It is recorded in 39 cases, and the subjoined table shows the number of cases for the various quinquennial periods.

Table of cases occurring in the Quinquennial Periods between the ages 25 and 75.

Age	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74
Number of cases ...	1	1	1	3	16	8	3	3	2	1
Percentage ...	2·5	2·5	2·5	7·7	41·02	20·5	7·7	7·7	5·1	2·5

The accumulation of 24 cases out of the total of 39 cases during the age period of the climacteric is striking.

Civil Condition and Fertility.—Of 40 cases in which the civil condition is known, 30 were in married women and 10 in single women. The percentages 75 per cent. and 25 per cent. respectively are roughly those of the female population as given in the Registrar-General's returns.

Of the 30 married women 14 (46·6 per cent.) had at one time or another borne children, and averaged each 4·85 full-term children. Their fertility is better seen in the following list, where it is shown that 41 (60·3 per cent.) of the children are from 4 women only :—

Uniparous = 5 women
3-parous = 1 woman
4- ,, = 1 ,,
5- ,, = 3 women
8- ,, = 2 ,,
11- ,, = 1 woman
14- ,, = 1 ,,

Of the above women 7 had further pregnancies which did not go on to full term. These 7 women had between them 11 miscarriages as follows :—

1 miscarriage in the case of 4 women
2 miscarriages ,, ,, 2 ,,
3 ,, ,, ,, 1 woman.

Catamenia.—The average age of onset was 14·9 years, the extremes being 12·5 and 18 years.

The average duration of menstrual life was, in those cases obtainable, 30·5 years.

There is little information concerning irregularity of the catamenia. In only 1 case is this noted, and it had then lasted for three years. For the rest they were regular, suffered no excess of pain, and no excessive loss except in 1 case in which there was present in association a fibro-myoma of the uterus.

Menopause.—The menopause reckoned in 14 cases gave an average onset at 45·29 years. In 17 cases (41·5 per cent.) the disease occurred while they were yet in active menstrual life. In only 2 cases was the onset of the menopause synchronous with that of disease.

In 21 cases (51·2 per cent.) the climacteric had previously supervened.

Relation to Pregnancy.—In no case is there evidence of pregnancy having co-existed with carcinomatous disease of the ovary.

Heredity.—In 5 cases (12·2 per cent.) there is a history of "cancer" having occurred in the family. It is of little value.

Duration.—The duration is reckoned from the onset of the first symptom to the date of death. Cases in which operation appeared to delay the end have not been reckoned. In all 29 such cases have been obtainable, and the average duration calculated for such is 14·65 months. The two extremes are: the longest duration 41 months, and the shortest 6·5 months.

Clinical Details.

The first symptom is of various nature, is likely to be recognised early or late in the disease according to its nature and to the introspective sensibility of the subject, and, of course, further depends upon many factors which can only be designated as "chance factors," such, for example, as whether it early adheres to gut, or to the position of the ovary in the pelvis. A list of first symptoms in order of frequency is subtended:—

"Tumour" or "enlargement" of abdomen .	13 cases
"Wasting"	5 ,,
"Constipation"	3 ,,
Disorders of micturition	3 ,,
"Dragging pain" in lower abdomen . .	2 ,,
Sacral pain	2 ,,
"Bearing down" pain	2 ,,
Diarrhœa	2 ,,

In addition, in 2 cases the first indication was the onset of intestinal obstruction, for which they were urgently admitted. In 1 case symptoms of biliary colic with lithiasis masked the ovarian condition. In another case symptoms referable to the cerebro-spinal system withdrew attention from the ovary to the extent that ovarian carcinoma was unsuspected and only discovered post mortem.

Enlargement of the Abdomen was noted during the course of the disease in 30 cases (73·2 per cent.), and varied both in nature and degree. In some cases it was due to ascites, in others to enlargement from the presence of a neoplasmic mass, and in yet a third series it was due to tympanites.

It was associated with ascites in 22 instances, and the amount of ascites varied enormously from that simply demonstrable clinically to that amount necessary to enlarge an abdomen to a 44-inch girth.

Paracentesis was found necessary to relieve pressure or for other reasons in 9 cases, and repeated several times in 6 cases.

In association with enlargement of the abdomen, dilated, full, and tortuous superficial veins were noted coursing over the abdominal wall in 12 cases.

Dyspnœa, presumably induced by increased intra-abdominal tension, occurred in 7 cases.

Emaciation of greater or less degree was present in 30 cases. In 11 cases the note "markedly emaciated," in 15 cases simply the word "emaciation," and in the remaining 4 cases the description "somewhat wasted," is applied. In 7 cases it is definitely stated that the patient was of "well-nourished" appearance.

Pain in some form was present in 22 cases (53·6 per cent.). Its nature is very various, and it is usually an unimportant and very secondary symptom. In no case was the pain localised in the region associated with disease of the ovary.

Gastro-Intestinal Symptoms.

Vomiting occurred in 17 of the series (41·5 per cent.), in all of which the intra-abdominal conditions were mechanically altered by ascites or tympanites.

Constipation, noted in 14 cases (34·2 per cent.), was severe in 4 cases, in two of which it amounted to acute intestinal obstruction.

Diarrhœa was present in 4 cases.

The liver was palpably enlarged in 3 cases (7·3 per cent.).

Genito-Urinary Symptoms.

Micturition was affected in 7 instances as follows:—

Difficulty of micturition	in 2	cases
Pain on micturition	„ 2	„
Frequency of micturition	„ 2	„
Micturition less frequent	„ 1	case

The **Urine** is recorded as "abnormal" in 6 cases.

It contained blood in 2 cases
pus ,, 2 ,,
sugar ,, 1 case
albumen in 5 cases.

Vaginal Examination.—A mass is recorded as felt per vaginam in 25 cases. Its position varies for each case, according to the position of the ovary previous to disease or to the position newly taken up on account of its altered volume and weight. Thus it may be found on the right or left side, in the posterior fornix, as a mass only felt bimanually, or as a mass rising out of the pelvis.

Later stages are exhibited in infiltration of the pelvic floor and fixation of the uterus. In two cases a carcinoma of the rectum was diagnosed owing to the fact that the growth occupied Douglas' pouch, surrounded the rectum, and became fixed to the sacrum.

The character of the mass exhibits marked polymorphism, varies widely in volume at different stages of the disease and in the different cases, and apparently imparts a different sensation of density to the various observers. The only two characters presenting any constancy are (1) that of hardness or tenseness noted 13 times (52 per cent.) and (2) that of fixation of the mass observed in 12 cases (48 per cent.).

Abdominal Examination.—In 14 cases no tumour could be felt at the first palpation of the abdomen, but in 6 of the same cases a mass was discovered after paracentesis.

In considering the character of the tumour felt through the abdominal wall, it is to be remembered that in many instances a mass in the omentum or some other secondary growth is being felt.

As a rule the tumour is about the size of a "cocoanut," and in 11 cases there was more than one tumour palpable. In 6 cases there was an indefinite sense of resistance obtained on dipping through a layer of fluid. The tumour felt was in 23 cases (56·1 per cent.) hard, irregular in outline, with "bosses" or nodules.

The position of the swelling is more commonly in one iliac fossa (11 cases) or rising out of the pelvis in the mid-line (7 cases). In later stages masses may be felt in any part of the abdomen.

In 2 cases a nodule was felt in the anterior abdominal parietes, and was the only tumour palpable.

Pathological Details.

Of the 41 cases, 34 cases were examined post mortem, and were consequently fully explored as to the existence of secondary growths. The 7 remaining cases underwent operation, and in 5 of these cases secondary growths were noted.

The following table shows the relative frequency of metastases in the various organs, worked out as percentages of the whole series.

In only two cases was there an absence of some form of secondary growth. It will be noted that the large majority of metastases falls upon the peritoneum, omentum, colon, intestine, and liver.

Table of Secondary Metastases in 39 Post-Mortems or Operations on Cases of Ovarian Carcinoma.

	Cases.	Per cent.
Pelvic peritoneum	36	87·8
Supra-pelvic peritoneum	29	70·7
Omentum	24	58·5
Colon	21	51·2
Intestine	20	48·7
Liver	17	41·4
Uterus	15	36·5
Rectum	13	31·7
Diaphragm	10	24·3
Bladder	5	12·1
Spleen	4	9·7
Stomach	3	7·3
Pleura, visceral	1	2·4
parietal	7	17·1
Lungs, R	2	4·8
Both	1	2·4

		Cases.	Per cent.
Hypogastrium (Wall)		2	4·8
Heart		2	4·8
Kidney,	R.	1	2·4
	L.	1	2·4
	R. and L.	1	2·4
Veins.	Inferior Vena Cava	1	2·4
	Portal	1	2·4
	Left Iliac	1	2·4
Appendix		1	2·4
Supra-renal		1	2·4
Pericardium		1	2·4
Ureters		1	2·4
Pancreas		1	2·4
Mesentery		1	2·4
Rectus Muscle, Right		1	2·4

TABLE OF METASTASES, IN 39 CASES OF OVARIAN CARCINOMA, IN THE LYMPHATIC GLANDS.

Iliac glands	showed	metastases	in 22 cases	56·09 per cent.
Mesenteric	,,	,,	,, 21 ,,	51·2 ,,
Lumbar	,,	,,	,, 15 ,,	36·5 ,,
Hepatic-portal	,,	,,	,, 3 ,,	7·3 ,,
Mediastinal	,,	,,	,, 2 ,,	4·8 ,,
L. Axillary	,,	,,	,, 1 case	2·4 ,,

Sites of Primary Disease.—

The right ovary was primarily attacked in 11 cases.
The left ,, ,, ,, 13 ,,
The primary seat undetermined in . . 17 ,,

Both ovaries were affected at some time of the disease in 27 cases, and only one ovary in 11 cases. The remaining 3 cases supply no information on the point.

Macroscopical Characters of the New Growth.—The size of the primary growth did not exceed that of an orange in 8 cases, and in 5 cases the growth is described as a "very large" one. In 8 cases the ovaries were said to be lost in a mass of cancer occupying the pelvis.

In 13 cases there were present in the cancerous mass cystic spaces, due variously to "breaking-down" of the growth, colloid degeneration, and in 2 cases large cysts in association with a carcinomatous base.

In 9 cases only is the new growth described as a perfectly solid, encephaloid, firm tumour.

In 27 cases (65·9 per cent.) the broad ligaments are recorded as being extensively infiltrated by the primary growth. In 2 cases the cancer is described, post mortem, as a movable mass.

Further, in 3 cases the papillomatous nature of the new growth, and also of its secondary metastasis, is recorded as noteworthy.

Microscopical Characters of the New Growth.—In 12 cases there is existing material from which the type of cell in the growth can be determined. The relative frequency in respect of cell-type in these 12 instances is as follows :—

Columnar-cell carcinoma	8 cases.
Spheroidal-cell ,,	2 ,,
Endothelioma-type ,,	2 ,,

It is to be remarked that in no case is there a typical cubical-cell carcinoma. The nearest approach is a flattened columnar-cell type where it is probable that pressure has been in some measure the medium of change.

With regard to the endotheliomata, they would probably be classified by certain histologists as spheroidal-cell carcinoma. One is, in fact, so described by an earlier observer. But there are striking differences between the endothelioma here classified and the spheroidal-cell carcinoma, in the general arrangement of the growth, in the absence of all papillary processes, in the absence of any tendency to the formation of adenomatous spaces.

The columnar-cell growths may best be described as carcinomatous papilliferous cystadenomata. In all the arrangement is adenomatous, and in some there are perfect papillary processes lined by columnar epithelium, and enclosing a central fibro-vascular core. The malignancy is to be noted in the constant invasion of the stroma in some part of the microscopic field by masses of cells irregularly arranged, or by the reduplication of the layers of cells covering a papilla or lining an adenomatous space.

The relation of these growths to non-malignant papilliferous cystadenoma is difficult to decide. In two of the above cases, a year before death, operation disclosed a simple papilliferous cystadenoma. At the post-mortem the cases were certainly malignant. The subject is under further consideration.

In the secondary growths the primary type is, as a rule, reproduced. Wherever the edge of the secondary growth is cut, the invasion of the surrounding tissue by direct extension is well seen.

RESULTS.

Of the 41 cases, death supervened in 33 instances, and 8 were discharged. This gives a definite mortality of 80·52 per cent.; but it is to be remembered that 2 of the above cases occurred in 1908, and that in 4 other cases the patient was discharged as "relieved," not as cured.

Operation was performed in 24 cases (58·5 per cent.).
No operation was performed in 12 cases (29·3 per cent.).
No information concerning operation in 5 cases.

Of the 24 cases operated upon 16 died in the hospital (mortality 66·6 per cent.), and 8 were discharged. The same remarks as above here hold good in that 2 were within the last 12 months, and that 4 other cases were not considered to be more than relieved.

PRIMARY SARCOMA OF THE OVARY.

During the period under consideration 16 cases of sarcoma of the ovary are reported. Here, as in the case of carcinomata, difficulty in eliminating doubtful cases has been experienced. The custom of using the term sarcoma as synonymous with malignancy has resulted in certain instances in the most confusing classification in the registers. The present series is, in consequence, based entirely upon a report of sarcoma after microscopical examination of the diseased organ.

Age.—The age of incidence is calculated from the time of presentation for treatment. The following table shows the number of cases and their percentage for the various decennial periods 10 to 70 :—

Age	10 to 19	20 to 29	30 to 39	40 to 49	50 to 59	60 to 69
Number of cases	3	2	2	3	3	3
Percentage ...	18·75	12·5	12·5	18·75	18·75	18·75

In respect of the age it is interesting to note that the new growth is of somewhat different character according as it occurs before or after 40 years of age. In the young it is a more rapid, solid, richly-cellular growth ; in the old it is a comparatively long-standing condition, the malignant nature of which only became apparent upon removal.

State and Fertility.—Of the 16 cases 8 occurred in married women and 8 in single women.

Of the 8 married women 3 had never been pregnant, 4 had borne children, and of 1 there is no information as to pregnancy.

Of the 4 child-bearing women :—

1 æt. 52 had 10 children and 1 miscarriage.
1 ,, 48 ,, 3 ,, ,, 1 ,,
1 ,, 39 ,, 2 ,, ,, 1 ,,
1 ,, 26 ,, 0 ,, ,, 1 ,,

Menstrual History.—Of 10 cases the average age of commencement of the catamenia was 13·9 years. The extremes, 10 and 18 years, were the earliest and latest respectively.

Of 6 cases which had passed the climacteric the average age of cessation was 46 years. All, in the absence of natural causes of amenorrhœa, were regular. Pain at the periods is reported in 3 instances, and excessive loss in 2 cases.

The menstrual history of 6 cases attacked before the menopause shows a certain period of amenorrhœa preceding death or operation.

1 case æt. 17 had never menstruated.

1 case æt. 16 had 3 months' amenorrhœa previous to double ovariotomy.

1 case æt. 21 had 4 months' amenorrhœa previous to double ovariotomy.

1 case æt. 26 had 5 months' amenorrhæa previous to death.

1 case æt. 37 had 31 months' amenorrhœa previous to death.

In 2 cases, æt. 39 and 46 years, menstruation occurred respectively 1 and 2 weeks previously, although both ovaries were in each case extensively diseased.

Duration.—The duration of the disease is also found to vary with earlier or later life. Thus the average duration of 12 cases in which the date of the first symptom and that of death was known was 23·38 months, but the following table shows that the average duration is different for the different decennial periods:—

Age-period	10 to 19	20 to 29	30 to 39	40 to 49	50 to 59	60 to 69
Duration in months ...	9·7	8	15	13	36·5	21

These figures have only a rough value, especially in the case of the period 50–59, as there is not included a case known to have a swelling in the left iliac region for 7 years, and which upon operation proved to be a dermoid cyst undergoing sarcomatous change.

Clinical Details.

The symptoms of sarcoma of the ovary are those of a lump arising in the pelvis and soon contracting adhesions.

Enlargement of the abdominal girth is in this series the more prominent note, and this usually in association with ascites.

Enlargement of the Abdomen was present in 94·3 per cent., and varied in degree from marked distension causing dyspnœa in 21 per cent. and a girth exceeding 41 inches, to cases in which increase in size was just perceptible and accompanied by a slight degree of ascites :—

Ascites was present in 64·2 per cent. of the cases.

Paracentesis was performed in 1 case and repeated 12 times.

Swelling of the legs and feet was present in 4 cases, and was probably the result of obstruction to venous return.

The following table gives the symptoms recorded and their relative frequency :—

Swelling of abdomen	15	93·7 per cent.
Ascites	9	56·2 ,,
Abdominal pain	8	50·0 ,,
Wasting	8	50·0 ,,
Vomiting	5	31·2 ,,
Swelling of legs and feet	4	25·0 ,,
Constipation	4	25·0 ,,
Dyspnœa	3	18·7 ,,
Diarrhœa	1	6·2 ,,
Abdominal colic	1	6·2 ,,
Pain on defæcation	1	6·2 ,,
Frequency of micturition	1	6·2 ,,

Pathological Details.

Of the series 11 cases came to post-mortem, and 5 cases (in which no autopsy was performed) underwent laparotomy. In every case there was some secondary deposit. They occurred in the majority of cases in the mesentery, omentum, liver, and retro-peritoneal glands.

In the following table the sites of secondary growths and their relative frequency are given :—

TABLE OF SECONDARY GROWTHS IN 16 CASES OF SARCOMA OF THE OVARY.

Mesentery	5	31·2 per cent.
Omentum	5	31·2 ,,
Liver	4	25·0 ,,
Pelvic wall	4	25·0 ,,
Supra-pelvic peritoneum	3	18·7 ,,
Pelvic colon	2	12·5 ,,

Rectum	2	12·5	per cent.
Transverse colon	2	12·5	,,
Uterus	2	12·5	,,
Douglas' pouch	2	12·5	,,
Anterior abdominal wall	1	6·2	,,
Spleen	1	6·2	,,
Diaphragm	1	6·2	,,
Bladder	1	6·2	,,
Lung (R. lower lobe)	1	6·2	,,
Heart (base)	1	6·2	,,
Lymphatic Glands—			
Lumbar	4	25·0	,,
Mesenteric	3	18·7	,,
Iliac	2	12·5	,,
Bronchial	1	6·2	,,

Other Pathological Details.

Dilatation of the pelvis of the kidney occurred in 4 cases, and in two of these it was bilateral.

The ureters were dilated in 2 cases. In 1 case both ureters, in the other the left ureter only was dilated.

Symptoms of intestinal obstruction were present in 1 case, and were caused by constriction of the lumen of the colon by a surrounding and invading mass of growth,

The supra-renals were "cystic" in 1 case.

Site of Primary Disease.—The incidence of the disease upon the ovaries was:—

In 14 cases both ovaries at a certain period were the seat of sarcoma.

In 1 case the growth was limited to the right ovary.

In 1 ,, ,, ,, ,, left ,,

These two latter cases occurred, the one in the case of a woman, æt. 60 years, with a large cystic tumour with solid base; the other, in a patient, æt. 57 years, with a large papillomatous cyst the size of a football.

The determination of the ovary in which the disease was primary was in some cases difficult. The criteria employed were those of size at operation or autopsy in the case of both enlarged, or where both were of about equal size, clinical evidence, such as the original side of symptoms, and physical signs, etc. The result of such an enquiry gives:—

Primary sarcoma of right ovary . .	in 7 cases.
,, ,, ,, left . . .	,, 7 ,,
,, ,, ,, ovary undetermined	,, 2 ,,

Also in the 14 cases in which both ovaries were affected, the primary incidence appeared:—

In the right ovary	6 cases.
,, left ,, ...	6 ,,
,, ovary undetermined . . .	2 ,,

It has been impossible to determine at what period of interval the disease attacks the opposite ovary. The distinction of mere size indicates the widest variations, such that, in one instance, a primarily affected and larger organ, compared in size to a small "orange," has the opposite organ the size of a "golf-ball"; while in another instance a large primary growth the size of a "fœtal-head" has a secondarily affected ovary the size of a small "orange."

Of 11 cases which had been submitted to laparotomy, in 6 instances both ovaries were reported diseased, and in 5 cases only one ovary was affected. Subsequent autopsy revealed disease of the other organ in 3 of the 5 cases.

Macroscopical Characters of the New Growth.—In volume the primary ovary was in more than half the cases (63·3 per cent.) large, and reported as being the size of a "football," "adult-head," 25 cms. diameter, etc. In no case was it apparently less than 12 cms. diameter at the time of autopsy or operation.

The secondarily affected organ presented more extensive variations in volume, ranging from that of double the normal size to that challenging the primary mass.

In form the growths were either round and occasionally lobulated or moulded between viscera and the pelvic boundaries. The character exhibits marked polymorphism from that of a large multilocular cyst to a solid firm white tumour. Between the two extremes are conditions described when viewed in section as of a "soft," of "creamy consistency," "honeycombed by hæmorrhages," "minutely cystic with clear contents," "fibro-cystic," "cysts with bloody colloid material," etc., and being of "reddish-white," "yellowish," "dark" or "mottled with hæmorrhages" in colour.

The following extracts may aid to a clearer picture :—

Case 2.—"R. ovary. A solid, firm tumour 25 cms. diameter on section, soft, yellowish, honeycombed by hæmorrhages and softenings."

"L. ovary similar."

Case 4.—"R. ovary. A hard, nodular mass of new growth, extensively adherent on section; solid substance, firm, yellowish, and in places caseating. Many small thin walled cysts with clear yellow fluid, and in walls of which are miliary nodules of new growth."

"L. ovary similar, but less adherent."

Case 5.—"R. ovary. A rounded tumour, size of a cocoanut, slightly adherent to R. Broad ligament—in parts finely nodular like a papillomatous growth, especially above in 2 small nodules attached to mesentery. On section: soft with a few cysts, one part vascular and translucent, other parts soft and distinctly myxomatous."

Case 6.—"L. ovary. A large multilocular cyst size of 'football.' In its interior many smaller cysts; fleshy and sessile intracystic papillomata. At base of larger cyst a lobulated mass of new growth."

Microscopical Characters.—Material for microscopic examination is obtainable in respect of 7 cases. Of the remainder the type of sarcoma is not specifically mentioned in 5 cases, though the diagnosis was founded on microscopical examination.

The relative frequency of the different cell types is here shown :—

Round-cell	4 cases
Spindle	3 ,,
Mixed spindle and round-cell .	3 ,,
Myxo-sarcoma	1 ,,
Cell type not specified . .	5 ,,

The growths are, as a rule, richly cellular, and little broken up by strands of fibrous tissue.

The iliac glands in one case show widespread infiltration by the sarcoma cells.

RESULTS.

Of the series 12 cases actually died in hospital (mortality, 75 per cent.). There were discharged 4 cases; but of these, in 1 case an irremovable hard nodule was left on the pelvic wall, in a second case a metastatic nodule appeared in the hypogastrium before discharge, in a third case the omentum and peritoneum contained secondary growths at operation, and in the fourth case operation was performed six months ago, so that the mortality probably exceeds 75 per cent.

PAPILLIFEROUS CYSTADENOMA OF THE OVARIES.

In the records of the Middlesex Hospital for the years 1854–1908 are found reports of 50 cases of papilliferous cystadenoma. These cases are here statistically considered.

Age.—The age is that on presentation in hospital for treatment upon the first occasion, and where definite information of treatment being received for the same disease at another hospital has been recorded, the age at that time is taken.

It is to be remarked that later cases (in the years 1896–1908) include none under 34 years of age, whereas previous to this period the cases are more numerous.*

The youngest case was a single girl æt. 24, very definitely reported as a multilocular cystadenoma.

The most advanced age recorded is that of a woman of 71 years. The mean age of presentation for treatment is 44 years, and from the following table it will be seen that the majority of cases occur between the 40th and 60th years.

Age	20 to 29	30 to 39	40 to 49	50 to 59	60 to 69	70 to 79
Number of cases	5	6	8	17	8	1
Percentage ...	11·1	13·3	17·7	37·7	17·7	2·2

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* The reason for this is not quite obvious; possibly it depends upon the fact that a condition which is clinically "non-malignant cystadenoma," histologically may be a malignant papilliferous columnar-cell carcinoma. It affords an illustration of the difficulty met with in assigning individual cases to either the malignant or the non-malignant group.

Civil Condition and Fertility.—Of the 50 cases 35 were in married women (76·1 per cent.), and 11 (23·9 per cent.) were in single women. In 4 instances the civil condition is not furnished in the reports.

Information concerning fertility is given in 25 cases of married women. Of these 25 cases 7 (28 per cent.) were sterile, and 1 case had never given birth to a living child. The remaining 17 women had between them 45 children (average 2·59). In the subtended list the degree of fertility is seen.

Sterile	7	women, 28 per cent.
Fertile	17	,, 68 ,, ,,
Uniparous	5	women
2-parous	6	,,
3- ,,	3	,,
4- ,,	1	woman
6- ,,	1	,,
9- ,,	1	,,

Among the married women were 7 (28 per cent.) who had been pregnant, but the pregnancy ended in miscarriage or abortion.

There was 1 miscarriage in the case of 5 women.
There were 2 miscarriages ,, ,, 1 woman.
,, ,, 5 ,, ,, ,, 1 ,,

Menstrual History.—The average age of onset of the catamenia calculated from 23 cases was 14·4 years. The extremes of variation were 11 and 19, earliest and latest respectively.

Irregularity of menses is noted as present in 6 cases, in which there were fibro-myomata of the uterus in 3 cases, and an intra-uterine polypus in 2 cases. There is in the reports no evidence to show that the disease of the ovary had any clinical effect upon the catamenia. In no case in which the disease became evident previous to the menopause is specific mention made of amenorrhoea.

Cessation of Menstrual Life.—The average of 20 cases where the time of onset of the menopause is signalised is 46·65 years.

The mean duration of menstrual life where such could be reckoned was 32 years.

Relation of the Disease to the Menopause.—In 40 cases sufficient data are given from which to calculate the relation of the disease to menstrual life.

In 24 cases the menopause is definitely recorded as having been passed. These include 3 cases in which the climacteric occurred at 35, 40, and 42 years respectively.

In 14 cases the disease manifested itself in the course of active menstrual life.

In only 2 cases is it recorded that the patients were actually passing the climacteric.

Heredity.—On this point there is little to record. The whole series contains two notes, one of an aunt having died of "cancer" (site not stated), another of a mother dying of a "tumour of the chest."

Duration.—The duration of the disease has been reckoned as the period between the subjective recognition of the first symptom and death. Cases which were operated upon have not been included. There are 10 cases not operated upon, and the average duration was 17·3 months.

The duration in those cases operated upon previously to 1898, calculated for 12 cases, was 11·7 months, and for those operated upon since that period and yet dying in hospital the duration calculated for 4 cases was 16·5 months.

Even in cases which have not been operated upon the duration is only "apparent," for the mass may reach to a considerable size in the absence of some symptom calling the patient's attention. This is more applicable in the case of cystadenomata than in strictly malignant growths.

It is necessary to divide the cases operated upon into two divisions, "early" and "late," since the "early" group are markedly affected by a faulty operative technique coincident with the period under consideration.

Clinical Details.

The first symptom recorded with its relative frequency is given in the subtended table.

"Enlargement" of abdomen .	26 cases,	52 per cent.
Pain in lower abdomen . .	4 ,,	8 ,, ,,

Troubles of micturition . .	3 cases,	6 per cent.
Wasting	1 ,,	2 ,, ,,
Vomiting	1 ,,	2 ,, ,,
Constipation	1 ,,	2 ,, ,,

Of the various symptoms during the course of the disease enlargement of the abdomen occupies the first place. It was present in 43 cases (86 per cent.), and in 29 cases was associated clinically with ascites, and this often to such a marked degree that the abdominal girth one inch below the umbilicus is recorded as being as much as 47 inches, $43\frac{3}{4}$ inches, and 41 inches in some cases, and in the majority exceeding 37 inches.

In 14 cases *paracentesis* was performed, once in 9 cases, 3 times in 2 cases, 5 times in 2 cases, and 25 times in 1 case. The average quantity of fluid withdrawn was 15 pints.

Swelling of the legs and feet was noted in 8 cases (16 per cent.). It generally appeared in the later stages of disease, and was due either to the presence of a mass or to ascites obstructing the venous return from the legs.

Dilatation of the superficial veins of the abdomen was recorded in 8 cases (16 per cent.).

Pain is recorded in 23 (46 per cent.) cases, but appears to be slight and due to secondary causes. Thus it is variously cited as "due to simple stretching of the abdominal walls" "of colicky nature," "pain in the back," and "painful sensation of weight."

Vomiting is present as a late symptom, always in association with marked enlargement of the abdomen as the result of ascites or tumour.

Wasting is noted in 19 cases (38 per cent.), and is found most markedly in the cases leading to incomplete intestinal obstruction.

Constipation is present in 24 per cent. of cases. In several cases it is a manifestation of increasing yet incomplete obstruction of the gut.

Troubles of Micturition.—Difficulty in passing urine is noted in 4 cases, frequency in 5 cases, and pain during the act of micturition in 5 cases.

Vaginal Examination.—In 23 instances there are notes of vaginal examination, and in these the uterus was normal, free, and mobile in 6 cases, was drawn up by the mass in the abdomen in 3 cases, and was pressed down and found low in the pelvis in 2 cases. It was fixed and immovable in 6 cases.

A mass in different cases was felt through the posterior fornix, through the right fornix, through the left fornix, and through the anterior fornix. This mass is described as "fluctuating," "cystic," "movable" or "fixed," "solid," "irregular," "hard like a fibroma," "round," "elongated," and varying in size from that of a large mass inseparable from the abdominal tumour to that of an "orange," or, as in one instance, a small nodule in the posterior fornix. On four occasions it was described as blocking up the pelvis.

Abdominal Examination.—Of 42 cases in which the clinical details are given, 33 cases (78·5 per cent.) manifested a definite abdominal tumour. In 4 cases a tumour, which was found post-mortem, was obscured during life by ascites, in 2 other cases tympanites rendered palpation unsuccessful, and in 2 cases the tumour was only felt bimanually.

The tumour may assume any of the characteristics of an abdominal swelling; being fluid with a distinct thrill, or a condition offering only local fluctuation, hard, soft, "bossy," and irregular. In shape and size it may vary from that of a well-defined pelvic mass to a tumour stretching from the pelvis to the costal margin. In 13 (30·9 per cent.) cases the tumour was more or less unilateral. It was described as a definite central tumour in 2 instances, and as movable in only 7 (16·6 per cent.) instances.

The earlier the condition is seen the more likely it is that the tumour will be felt in one or other iliac fossa.

There is little doubt that some of the tumours described were secondary masses in the omentum, or adhesions acquired by the original tumour.

In 3 cases the tumour is described as resonant, and in the remaining cases as centrally dull to percussion, but radiating laterally into resonance.

A "thrill" was obtainable bimanually in 3 cases.

Pathological Details.

In 36 per cent. one ovary only was diseased, and in these cases the right ovary was affected in 6 cases, the left ovary in 9 cases. In 3 cases no specific mention is made of the ovary affected.

In 32 cases (64 per cent.) both ovaries were affected.

The primary site of disease was the right ovary in 11 cases.

The primary site of disease was the left ovary in 8 cases.

The primary site of disease was indeterminable in 13 cases.

The growth is described as large in 30 per cent. of the cases. The cases for the last ten years, however, indicate tumours of much less volume than those of the anterior period, and in this respect offer a contrast to the observation by Dr. Campiche in the case of tumours of the breast.*

Macroscopically the growth is an irregular, more or less spheroid tumour, containing numerous cysts, or composed entirely of one multiloculated cyst. The tumour is usually pedunculated, the pedicle being formed by the mesovarium or in the larger growths by the broad ligament. Near the point of attachment of the cyst a variable amount of solid tissue is present, which as a rule projects into one or more of the loculi, either in the form of papillae, or in that of nodular plaques in the cyst wall.

The intracystic growth varies from the finest slender, easily friable dendritic processes, to a warty condition in which the growth is typically a cauliflower-like excrescence, or a condition may obtain in which there is apparently a simple mass of solid growth, which, however, on section shows small cystic spaces. The contents are either a transparent, colourless, or a dark blood-stained mucoid material.

Microscopical Character of the Growth.—The primary growth in this class of case exhibits marked differences in microscopical character. In one variety a typical papillomatous cystadenoma is present. That is to say, processes are present of a fibrous stroma carrying blood-vessels, which is covered by a single layer of columnar epithelium, staining well both in respect of its cytoplasm and its actively mitotic nucleus. These processes project into cystic spaces of various size and shape, lined by an epithelium identical in character with that covering the processes.

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* 'Archives of Middlesex Hospital,' vol. v., p. 92.

In another variety similar gross characteristics are present, but the single layer of columnar cells is replaced by a layer of spheroidal cells.

In a third variety the papillary processes are entirely absent, and the growth is a cystadenoma, with well-marked fibrous stroma, in which the cysts vary enormously in size, and in which the layer of lining epithelium is columnar or cubical.

Secondary Growths.—As all the cases in this series were either operated upon, or examined post mortem, it follows that the question of secondary formations is one upon which considerable reliance can be placed. Of the 50 cases under consideration, 14 cases showed no secondary nodules, and 4 of these cases underwent post-mortem examination, while the remaining 10 cases were operated upon. The probability of any secondary growth being overlooked in the case of papilliferous cystadenoma is relatively small, since in the majority of cases they occur upon the pelvic peritoneum or omentum.

The commonest site of secondary growth (72 per cent. of cases) is the pelvic peritoneum, affecting in a large majority of cases Douglas' pouch, but rarely being found in the vesico-uterine pouch, and still less rarely upon the lateral pelvic walls. Hence the more dependent parts are those of election. This is borne out by the fact that for 28 cases of infection of Douglas' pouch, only 11 cases were found in which the uterus was the seat of metastases, and of these, 9 cases showed growth in Douglas' pouch as well.

Another striking feature is the readiness with which the omentum (27 cases) becomes involved, and also that in 13 cases deposits occurred upon the liver.

These secondary formations are generally described as superficial implantations, easily shelled-out, and never penetrating to any depth. Their appearance in large measure corresponds to that of the solid portions of the primary tumour. They are, in consequence, described as "warts," as "papillomatous-looking growths," as "flat lenticular nodules," or as "small cystic rounded nodules." The only apparent exception to this statement obtains in the case of the omentum, where often there is a large conglomerate mass, inextricably blended with a matted omentum or mesentery, and in some instances exceeding the size of the original focus. Nevertheless, even these masses, on section, show their resemblance to the primary tumour.

TABLE OF SECONDARY GROWTHS, SHOWING THE RELATIVE FREQUENCY OF LIABILITY OF THE VARIOUS SITES.

(*a*) **Peritoneum.**		
Douglas' pouch. . . .	28 cases	56 per cent.
Supra-pelvic peritoneum	25 ,,	50 ,,
Omental . . .	27 ,,	54 ,,
Intestinal . . .	14 ,,	28 ,,
Colic	14 ,,	28 ,,
Hepatic	13 ,,	26 ,,
Uterine	11 ,,	22 ,,
Diaphragmatic . .	8 ,,	16 ,,
Mesenteric . . .	9 ,,	18 ,,
Splenic	4 ,,	8 ,,
Rectal	4 ,,	8 ,,
Gastric	2 ,,	4 ,,
Parietal	2 ,,	4 ,,
(*b*) **Glands.**		
Iliac	3 ,,	6 ,,
Lumbar	3 ,,	6 ,,

The vagina was never found to be affected, nor the gut perforated by growth.

Double hydronephrosis was noted in 4 cases, and dilatation of the left ureter in 1 case.

The generally received opinion that papilliferous cystadenomata vary considerably in malignancy, some at least being apparently non-malignant, while others show a malignancy that culminates in death, is borne out by histological examination of the growths. In the minority (28 per cent.) of the cases no secondary growth of any description was found ; in the remainder secondary growth was present, and varied from a small mass in the fringe of the omentum, to numerous growths in the peritoneal cavity.

RESULTS.

The mortality in the whole series of 50 cases was 32 (64 per cent.). But in considering the mortality it is necessary to divide the cases according as operation was performed in the early days of ovariotomy or recently.

Thus of 23 cases operated previously to 1896, 15 cases (65·2 per cent.) died, and the cause of death in some at least of these cases must be attributed to faulty operative technique. For example, at the autopsy suppurative peritonitis was found in 8 instances, and the cause of death in 1 case was pulmonary embolism, and in another case failure to establish a satisfactory colotomy.

Since the year 1896 15 cases have been operated, and the mortality was 33·3 per cent.

MALIGNANT DISEASES OF THE BREAST: A STATISTICAL STUDY BASED ON THE RECORDS OF THE MIDDLESEX HOSPITAL FROM 1904 TO 1908 INCLUSIVE.

By H. BECKTON.

I. INTRODUCTION.

The object of the present Paper is to compare the results of a study of the last five years' cases of malignant disease at the Middlesex Hospital with those of the investigation of all the previous cases at the same hospital as set forth in the Fifth Volume of these Archives (Fourth Cancer Report), 1905. That investigation dealt with 1,976 cases occurring during the years 1747 to 1903 inclusive; the present communication is based upon a much smaller but much more compact body of cases, viz., the 481 occurring during the five years 1904 to 1908 inclusive.

For the sake of ready comparison, the headings of sections and paragraphs in the present paper correspond with those given in the previous investigation.

II. GENERAL STATISTICS.

Relative Frequency in the Two Sexes.—Of the 481 cases of malignant disease of the breast here considered, 477 occurred in females and 4 in males. Although the latter number is too small to be of much value, it may be remarked that the ratio here found (120 to 1) is almost identical with that given by Roger Williams (117 to 1); a ratio which, however, is somewhat higher than that generally accepted, and decidedly higher than the 75 to 1 found in the previous paper.

Sarcoma.—Nine cases of primary and two of secondary sarcoma occur among the 380 cases microscopically diagnosed as malignant disease, and all in females; the ratio of primary sarcoma to total primary malignant disease of the breast in females being thus 1 to 42—a percentage of 2·3. This agrees closely with the percentage of 2·2 founded in the previous paper on macroscopical evidence, but differs markedly from the 7·7 per cent. based on histological examination. The figure (3·9 per cent) given by Roger Williams lies between the two microscopical findings.

The Relation of Malignant to Non-Malignant Growths of the Breast.

TABLE I.

Table showing the Number of Admissions for Malignant and Non-Malignant Growths of the Breast during the Years 1904 *to* 1908 *inclusive.*

Year	1904.	1905.	1906.	1907.	1908.
Cases of malignant disease	69	46	63	72	89
Percentage of total mammary new growths ...	80·2	78·0	67·7	80·0	86·4
Cases of non-malignant new growths... ...	17	13	30	18	14
Percentage of total mammary new growths ..	19·8	22·0	32·3	20·0	13·6

The same relative constancy is here observable as in the corresponding table of the previous paper. Taking the total number of admissions for malignant and non-malignant growths during the five years, viz., 339 and 92 respectively, the corresponding percentages 78·7 and 21·3 are found, which agree remarkably closely both with those calculated from the table of the earlier paper, viz., 77·7 and 22·3, and with those given by Roger Williams, viz., 81·6 and 18·4.

III. CARCINOMA OF THE BREAST IN FEMALES.

(A) Pathological Anatomy.

Site of Appearance of the Growth.

Primary Carcinoma.—The site at which this first appeared is given in 274 cases. In 141 the distribution was as follows:—

Upper and outer quadrant	77 cases
Upper and inner ,,	33 ,,
Lower and outer ,,	22 ,,
Lower and inner ,,	9 ,,

In 89 cases the distribution was as follows:—

Upper part of breast	29 cases
Outer ,, ,,	30 ,,
Lower ,, ,,	20 ,,
Inner ,, ,,	10 ,,

In 23 instances the situation was central (beneath the nipple and areola), and in 18 cases it appears to have been at the nipple itself. The remaining 3 cases are recorded as having their primary site in the axillary tail of the breast.

Reducing the cases of the 2nd series to terms of the first the following figures are obtained:—

Upper and outer quadrant	48 cases
Upper and inner ,,	21 ,,
Lower and outer ,,	14 ,,
Lower and inner ,,	6 ,,

Adding these to the 141 cases of the 1st series, the following distribution is arrived at for the 230 cases:—

Upper and outer quadrant	125 cases
Upper and inner ,,	54 ,,
Lower and outer ,,	36 ,,
Lower and inner ,,	15 ,,

Thus the percentage distribution of the 274 cases is as below; and the corresponding percentages in the previous and larger series are added for comparison.

TABLE II.

Table giving the Percentage Occurrence of Primary Carcinoma of the Female Breast, arranged according to the Site of Growth.

—	1904–1908. (274 Cases.)	1747–1903. (1,013 Cases.)
Upper and outer quadrant	45·6 per cent.	44·4 per cent.
Upper and inner ,, ...	19·7 ,,	16·5 ,,
Lower and outer ,, ...	13·1 ,,	12·2 ,,
Lower and inner ,, ...	5·5 ,,	6·2 ,,
Beneath nipple (central)	8·4 ,,	12·0 ,,
In nipple	6·6 ,,	7·5 ,,
Axillary tail of breast	1·1 ,,	1·0 ,,
Outlying lobule on sternum	—	0·2 ,,

Site of Secondary Carcinoma.—Secondary growth in the opposite breast was noted in 46 of the 412 cases of cancer of the female breast in which details are given as to the side first affected. In 17 instances the site of the metastases is given, the distribution being as follows:—

Upper and outer quadrant	2
Upper and inner ,, ...	3
Lower and outer ,, ...	1
Lower and inner ,, ...	–
Upper part of breast	1
Outer ,, ...	2
Lower ,, ...	2
Inner ,, ...	1
Beneath nipple (central)	4
Axillary tail of breast	1

These figures differ very markedly from those of the previous report already referred to (upper and outer quadrant, 10; upper and inner quadrant, 1; nipple, 1; central, 1—Total, 13). They are, however, very small, though they still to some extent support those obtained for primary disease, the metastases occurring in the upper part of the breast 7 times as against 3 times in the lower, and in the outer part 6 times as against 4 in the inner.

Number of Initial Nodules.—The results of the present investigation support the conclusion arrived at in the previous paper, viz., that the rule may be adopted that carcinoma of the breast is of unicentric origin. In one case the first sign of the disease noted by the patient was the presence of two separate lumps; on the other hand, in a case in which three discrete nodules were found in the same breast on admission, the patient had definitely noted one of these—the largest—first, and the others in turn subsequently.

The Side Affected.—Information is given on this point in 412 cases. The primary growth was situated in the left breast in 208, and in the right in 204 cases. The very small difference between these numbers is significant as indicating little or no difference between right and left breasts as regards liability to cancer.

In the 46 cases of secondary growth in the opposite breast the primary growth was situated in the left breast in 26 instances and in the right in 20 instances. These 46 cases represent 11·2 per cent. of the whole series of 412 cases here considered; in the earlier paper the corresponding percentage of secondary growths was 9·1, while the primary growth was situated more frequently in the right (73 cases) than in the left (64 cases). Figures are given in 29 cases as to the interval elapsing between the invasion of the first breast and that of the second. In 23 instances the interval is stated quite definitely, and the average is 36·2 months, which agrees with the 3 years found in the previous paper. In the remaining 6 instances, however, the secondary growth is recorded as having been noted within 9, 10, 18, 20, 22, and 48 months respectively of the onset of the primary; if these figures be counted without diminution (and they would doubtless have been higher had the observation of the secondary growth been left to the patient instead of having been made at the hospital) the effect would be to give for the whole 29 cases an average interval of 33·1 months. This figure lies between that arrived at in the previous paper of 1904 (3 years), and that cited as given by Gross (29·8 months). The longest interval recorded in the present investigation is 123, the shortest 2, months.

In the present investigation two instances have been found of two different primary growths originating in the same breast. In one of these instances the different growths formed two discrete masses; in the other case the histogenetically different elements were recognisable microscopically in the same section.

Ulceration.—Of primary growths, ulceration is recorded in 77 cases: 71 cases on admission and 6 subsequently. In 52 instances such details are available as to allow of the calculation of the time elapsing between the "onset" of the disease (i.e., the date at which the first sign or symptom was noted by the patient) and the appearance of ulceration; the average interval is found to be 30·3 months. This agrees very closely with the mean of the results arrived at in the investigation of three separate series of cases in the former paper, viz., 29, 29, and 34 months.

Size of Growths on Admission.—Indications of the size of the growths on admission are given in 234 cases, and classifying growths as being "small" if not larger than a "walnut" &c., "large" if equal in size to a "tangerine orange" or greater than this up to the size of a "cricket-ball" &c., and "very large" if equal in size to a "cocoanut," a "football," &c., it is surprising to find that "large" growths are not only very frequent, but actually form a considerable majority in these cases, the figures being

"Small"	75
"Large"	151
"Very large" or "Enormous"	8
	234

Retraction of Nipple.—This sign was present in 101 cases, i.e. in 24·5 per cent., a figure which agrees well with the 26 per cent. found in the previous paper. In the 368 cases in which details are given as to the onset of the disease, retraction of the nipple, alone or accompanied by growth or pain, constituted the first manifestation of the disease in 13 cases, i.e. 3·5 per cent. In the paper of 1905 retraction of the nipple was found to be the first sign in 3·8 per cent. of all cases (cp. p. 89).

Paget's Disease of the Nipple.—This is recorded as having been present in two cases (one definitely, the other with some doubt)—i.e. in 0·5 per cent., but was probably present as a precursor of carcinoma of the breast in a larger proportion of cases (loc. cit. p. 89). Independently of cancer of the breast 2 cases of Paget's disease were admitted to the Middlesex Hospital during the years 1904–8, giving a percentage of 0·5 as compared with the corresponding percentage of 0·64 given in the former paper.

De Morgan's Spots (Telangeiectases).—These were observed in 4 cases of carcinoma of the female breast, giving a percentage of 1·0 as compared with the 1·6 found in the paper of 1905.

Œdema.—Œdema of the arm occurred in 48 cases out of 412, giving a percentage of 11·6, which accords well with the percentage of 10·6 found in the previous paper. In 12 of the cases the time elapsing between the onset of œdema and that of the disease has been calculable, and the average interval has been found to be 41 months as compared with 50 months in the earlier investigation. Of these 12 cases, 8 died ultimately at an average interval of 13 months after the onset of œdema.

(B) SECONDARY GROWTHS IN CASES OF CANCER OF THE BREAST.

In the present series of cases 96 were the subjects of post-mortem examination. The distribution of the secondary growths in these cases is given below in tabular form, and the percentage numbers obtained from this series compared with those deduced from the table given in the previous paper. In that article it was remarked that in the construction of the table referred to, access was possible to both clinical and post-mortem registers; these have accordingly both been made use of in the following, but it is well to state here that consultation of the clinical records has affected the numbers to any considerable extent only in the cases of "axillary glands," "cervical and supraclavicular glands," "skin nodules," and "opposite breast."

TABLE III.

Table showing the sites of Secondary Growths in Cases of Cancer of the Breast examined Post-mortem.

—	Actual numbers Present Series (96 Cases).	Percentages Present Series (96 Cases).	Percentages Previous Series (470 Cases).
Lymphatic glands :—			
Axillary	70	72·9	75·2
Cervical and Supraclavicular	47	49·0	27·1
Pre-auricular	1	1·0	—
Bronchial	18	18·8	17·2
Lumbar	8	8·3	2·6
Portal	8	8·3	
Mesenteric	5	5·2	6·0
Aortic	4	4·2	—
Pelvic	3	3·1	—
Inguinal	5	5·2	2·9
Thoracic Duct	1	1·0	—
Pleura	17	17·7	34·0
Pericardium	6	6·3	8·7
Peritoneum and Omentum ...	4	4·2	7·9
Diaphragm	4	4·2	—
Skin (discrete nodules)	18	18·8	17·2
Opposite breast	26	27·1	18·1
Liver	51	53·1	45·1
Lungs	37	38·5	34·6
Suprarenal	11	11·5	7·4
Kidney	8	8·3	8·7
Ovary	7	7·3	5·1
Brain (and Meninges, 1905) ...	6	6·3	4·9
Pancreas	6	6·3	3·4
Intestine (and Stomach, 1905) ...	4	4·2	3·4
Thyroid	4	4·2	1·9
Uterus	4	4·2	1·1
Spleen	3	3·1	2·8
Vagina	1	1·0	—
Bones :—			
Ribs	9	9·4	8·7
Skull	9	9·4	3·8
Vertebræ	8	8·3	6·8
Femur...	7	7·3	6·0
Humerus	5	5·2	3·2
Sternum	4	4·2	0·2 (?)
Clavicle	2	2·1	1·9
Pelvis	1	1·0	1·1

Metastases occurred also in the following in the earlier series of 470 cases, but are unrepresented in the present set of 96 : Heart 2·3 (per cent.), Bladder 0·9, Facial Nerves 0 9, Medulla Oblongata 0·6, Scapula 0·6, Bones of Leg 0·4, Bones of Forearm 0·2, Fallopian Tubes 0·2.

The general correspondence between the two tables of metastases is very striking, especially in the cases of secondary deposits in the viscera and the bones. The following remarks may be made here :—

1. Almost exactly one-half of the cases examined post mortem (47 out of 96) are recorded as having undergone one or more operations before death ; with this fact are probably associated, to some extent, the large increase in the numbers of metastases near the site of the original growth—cervical and supraclavicular glands, opposite breast—and the slight increase in the numbers of metastases elsewhere in general.

2. Microscopic examination in doubtful cases of secondary deposit must also be considered as partly responsible for the general increase observed in the numbers of metastases.

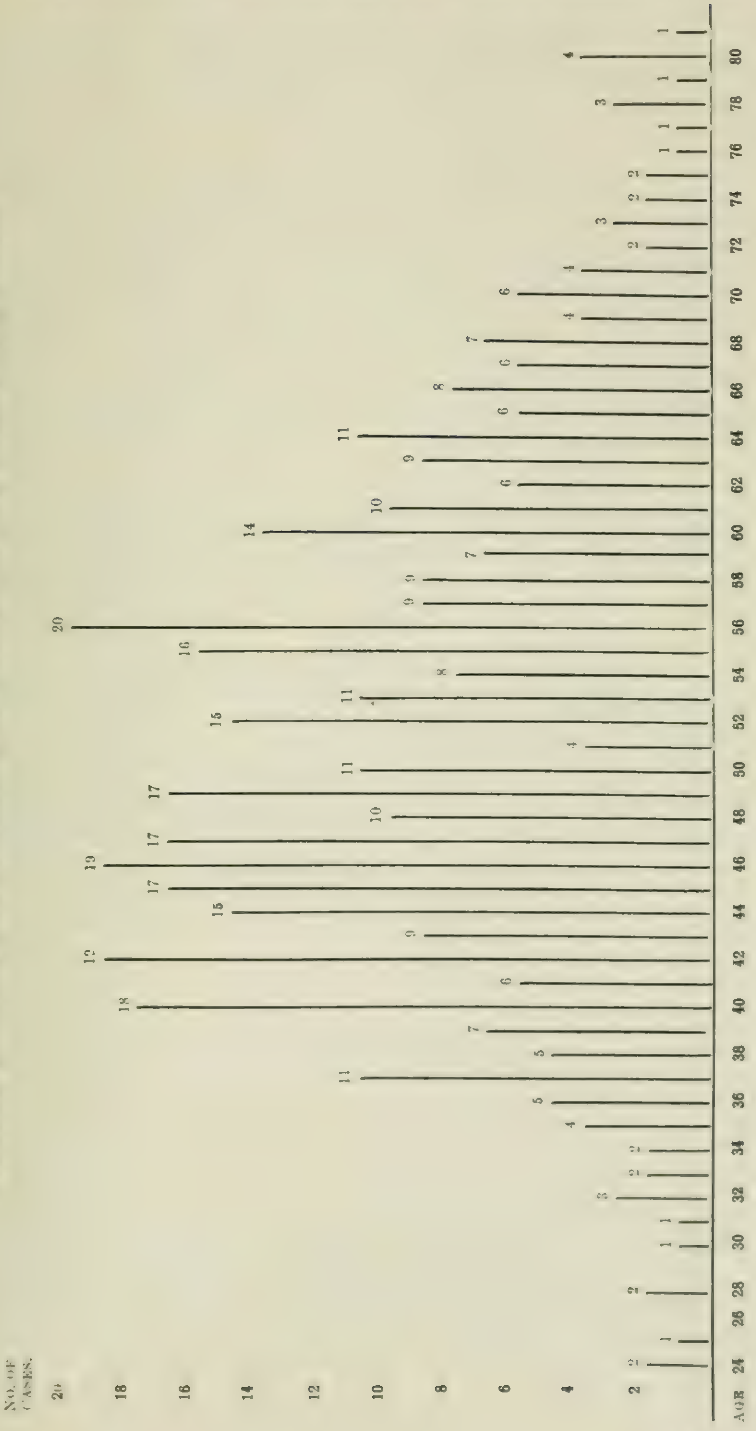
3. The priority of the liver over the lungs as a site of secondary growth, noted in the earlier investigation and indicated in the above table, is still more marked in the present series of cases.

4. The high positions occupied by the suprarenal gland and the ovary as seats of secondary growth, remarkable on account of the small size of these organs, in the table of 1905, are emphasized in the present series, especially in the case of the suprarenal, which here comes next to the liver and the lungs among the viscera. The position held by the spleen, on the other hand, remains low.

(C) CLINICAL OBSERVATIONS.

Age.—Information is given on this point in 414 cases of cancer of the female breast. As in the paper on "Cancer Ages" in the Fifth Volume of the Archives, the ages of onset are here taken as those of the patients at the time when they first came under observation. The age-incidence is shown in full detail in the accompanying diagram ; in the present series of cases the ages ranged from 24 to 81 years, with an average of 52·1, these figures comparing with a range from 22 to 89 years, and an average of 51·4 in the earlier and larger series

Diagram showing Age-Incidence of Cancer of the Breast (414 Cases).



The percentage occurrence in quinquennial age-periods is given in the following table, and compared with that found in the previous investigation :—

TABLE IV.

Table showing the Percentage Occurrence of Cancer of the Breast in Quinquennial Age-Periods.

Age	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69	70 to 74	75 to 79	80 to 84	85 to 89
Present Series of Cases ...	0·5	0·7	2·2	7·7	16·2	19·3	11·8	14·8	12·1	7·5	4·1	1·9	1·2	0·0
Earlier Series of Cases ...	0·1	1·0	4·0	8·2	14·8	16·9	16·3	14·2	12·3	6·8	3·4	1·4	0·2	0·2

The earlier series, as is to be expected from its comprising a much larger number of cases, shows a more even rise and fall; but the general correspondence is fairly close, and in particular the two series agree in showing the actual maximum case-incidence as occurring in the quinquennium 45–49

Civil State.—In 412 cases details are given on this point, and it is found that 310 patients were described as married, and 102 unmarried, giving percentages respectively of 75 and 25, which agree closely with the 77·2 and 22·8 found in the previous paper, and with the ratio of married and unmarried females in London. The married are sub-divided as follows :

Married (no details as to children) . . .	90
Married with no children	37
,, ,, 1 child	34
,, ,, 2 children	33
,, ,, 3 ,, ...	35
,, ,, 4 ,, ...	21
,, ,, 5 or more children . . .	60
Total	310

Occupation.—Of the 310 married and 102 unmarried women, 297 and 60 respectively were engaged in housework, this term being held to include domestic service (2 and 9 cases respectively), cookery (4 and 10), and charing (6 and 0), as well as those cases in which no occupation is mentioned (21 and 10).

The remaining 13 and 42 respectively were engaged in various occupations, those of dressmaker (4 and 13), schoolmistress (0 and 5), and nurse (2 and 3) being most numerously represented.

Pregnancy.—Cancer developing in the breast during pregnancy is recorded four times in the present series, the appearance of a "lump" in the breast during that period having been in each instance the first sign of cancer. In 3 cases pregnancy took place in patients suffering from cancer of the breast, and in each of these the whole period up to child-birth was included in the interval elapsing between the first sign (in each instance a "lump" in the breast) and admission to the Hospital.

Lactation.—As in the previous investigation, satisfactory details are given in comparatively few cases, and the information gleaned is of much the same nature, as may be seen from the following table :—

TABLE V.

Details as to Lactation in Cases of Cancer of the Breast.

—	Present Series.	Earlier Series.
Number of cases in which adequate information is given	38	74
Patients suckled children and had no trouble with breasts	25	43
Patients did not suckle children at all	5	5
Patients suckled children only with breast subsequently cancerous	1	6
Patients suckled children only with opposite breast	3	13
Under-lactation	2	4
Over-lactation	1	3
Cancer developed during lactation	2	9

The figures in these two series agree about as closely as might be expected under the circumstances. It should be mentioned that the two instances of under-lactation (two months and three months respectively, and stated as being due to no trouble with the breasts) in the present series are independent of three others in which the actual growth of the cancer put a period to suckling; these three cases are identical with three of the four mentioned in the preceding paragraph as cases in which cancer developed in the breast during pregnancy. In the case of over-lactation the patient was suckling a two-year-old child when "the milk stopped, and the breast went quite hard"; this case is identical with one of the two given in the last line of the table.

Menstruation.—It is seen from the diagram showing the age-incidence of cancer of the breast in the present investigation that in the 414 cases in which the age of onset is given this took place before the average age of the menopause (taking this as 47 years) in about one-third, and after in about two-thirds, of the total number of cases. It is also seen that 255 cases, i.e. nearly two-thirds of the total number, fall within ten years of this average age.

More exact information is, however, obtained from those cases, numbering 115, in which the ages of both menopause and onset of cancer are available; from the data given in these cases the following table has been constructed :—

TABLE VI.

Table showing the Number of Years elapsing between the Menopause and the Onset of Cancer of the Breast.

Number of years	0	1 to 5.	6 to 10.	11 to 15.	16 to 20.	21 to 25.	26 to 30.	31 to 35.	36 to 40.	41 to 45.
Number of cases ...	14	27	16	16	20	12	7	2	0	1

From this table the onset of cancer appears to take place later than 10 years after the menopause as often as within the 10 years following that event; or, again, as many women get cancer of the breast more than 15 years after the menopause as during the 5 years following it. These figures are especially striking when the diminution of the number of women alive at later ages is taken into consideration, and discount any idea of connection between the menopause and the onset of cancer of the breast which may be suggested by a consideration only of the average ages at which these two events take place.

Family History of Tuberculosis and Malignant Disease. History of Previous Injuries.—In the present investigation a definite family history of tuberculosis is found in 75 of 414 cases of cancer of the breast, i.e. in 18·6 per cent. Of malignant disease there is a family history in 51 cases, i.e. 17·4 per cent. A history of previous injuries such as blows and falls is given in 46 cases, or 11·1 per cent. These three figures correspond with percentages of 18·6, 15·6, and 17·9 respectively in the previous paper.

Homologous heredity (i.e. family history of malignant disease of the breast) is recorded in 21 cases of the 414, giving a percentage of 5·1 as compared with 2·6 in the paper of 1904.

Further observations may be summed up in tabular form as follows :—

TABLE VII.

Table showing the Numbers of Cases with Family History of Tuberculosis and Malignant Disease and History of Previous Injury, expressed as Percentages of the Total Numbers of Cases of Cancer of the Breast.

—	Present Series.	Previous Series.
Malignant disease alone	12·3	10·5
Tuberculosis alone	13·0	12·6
Injury alone	7·9	12·4
Malignant disease and Tuberculosis	3·4	2·5
Malignant disease and Injury	1·0	2·0
Tuberculosis and Injury	1·5	2·9
Malignant disease, Tuberculosis, and Injury ...	0·7	0·6

While the general agreement of the results of the present and the earlier investigations is thus apparent, records of previous injury are less frequent than was formerly the case.

General Health and Emaciation.—Information as to condition on admission to the hospital is given in 228 cases; these have been classified as "Emaciated" 34, or 14·9 per cent. of the cases, "Fairly well nourished" 58, or 25·4 per cent., and "Well nourished" 136, or 59·6 per cent. The corresponding percentages found in the previous paper are respectively 46·4, 3·4, and 50·2; the discrepancies may be partly due to improvement in the conditions of life among the poor, but are probably also due in part to different interpretations placed by the writers of the present and the earlier papers on similar descriptions as regards emaciation.

Subdividing the well nourished according to the duration of the disease the following percentages are obtained and compared with those found in the former investigations:—

TABLE VIII.

Table showing the Diminishing Number of Well-Nourished Patients with Increase in Duration of Cancer of the Breast.

Well-nourished in the	Present Series.	Previous Series.
1st year of disease	24·1 per cent.	30·2 per cent.
2nd " "	12·7 " "	6·8 " "
3rd " "	7·4 " "	5·0 " "
4th and later years	15·4 " "	8·2 " "
Total	59·6 " "	50·2 " "

The percentages in the two series of cases show the same general tendencies, and the conclusion arrived at in the earlier paper, viz., that emaciation is a late symptom in carcinoma of the breast, is here confirmed.

Pain.—In 288 cases definite reference is made to this point; in 247 (i.e. in 85·8 per cent. of these cases) pain is recorded as being present, and in 41 (i.e. 14·2 per cent.) absent. These percentages compare with 95·5 and 4·5 respectively in the former paper.

Of the 247 cases in which pain was present it is mentioned as being but slight in 41 cases, and of the remaining 206 it is described as "shooting" in 51 cases, other epithets such as "stabbing," "piercing," "darting" and "dragging." "aching," being each met with much less frequently. Investigation of the present series of cases, however, has yielded no suggestion as to any connection between the nature of the growth and the presence or character of the pain associated with it.

Of the 41 cases in which pain was absent, in 28 the first sign of the disease had been noted not more than one year previously, 11 of the 28 growths being "small," 10 "large," and 1 "enormous"; of the remaining 13 cases the growth was "small" in 3, "large" in 5, and "very large" in 1. Thus while pain is present in the majority of cases of cancer of the breast and sometimes constitutes its first manifestation, its absence appears to be independent, to a large extent at any rate, of both the duration of the disease and the size of the growth.

The First Sign noticed by the Patient.—In the great majority of cases included in the present investigation the first signs and symptoms observed by the patients have been carefully recorded and are classified and compared with those found in the earlier investigation as follows:—

TABLE IX.

Table showing the First Sign noticed by the Patient in Cases of Cancer of the Breast.

—	Present Series (378 Cases). Actual Numbers.	Present Series (378 Cases). Percentages.	Previous Series (500 Cases). Percentages.
A "lump" in the breast	263	69·6	63·0
A "lump" in the axilla first	3	0·8	2·0
Growth and pain together	42	11·1	11·4
Pain alone	30	8·0	14·4
Discharge or bleeding from nipple ...	16	4·2	1·6
Retraction of nipple (v. infra) ...	13	3·5	3·8
Ulceration	3	0·8	0·4
Sense of itching...	2	0·5	1·6
Redness or puckering of skin	2	0·5	1·0
Miscellaneous	4	1·0	0·8

Of the 13 cases in which retraction of the nipple is given in the above table as the first sign this phenomenon was observed alone in 6 cases, but was accompanied by a "lump" in the breast in 6 others, and by pain in the remaining instance. The 4 "miscellaneous" signs include those recorded as "a pimple on the nipple," "abscess," "dropping of the breast," and "contraction of the breast," respectively.

IV. CARCINOMA OF THE BREAST IN MALES.

Only 4 cases of carcinoma of the male breast are recorded at the Middlesex Hospital during the five years covered by the present investigation, all of these being primary. Two of the cases were admitted to the Hospital for local recurrence after operation; one of these had undergone operation one year previously at the Middlesex Hospital in 1903 (thus being included among the cases dealt with in the earlier investigation), the other, according to the patient's own account, 14 years previously.

Side Affected.—In 3 instances the left breast was the site of the growth; in 1 the right. In the previous paper the numbers were: right 11, left 4; thus in both papers the disadvantage of dealing with small numbers is well illustrated. Adding and allowing for the case which is counted in both papers, we get: right 12, left 6; this is still far from the slight preponderance of the right breast (53 per cent.) over the left (47 per cent.) found by Roger Williams in 71 cases of cancer of the male breast.

Site.—Recorded in 2 cases as central (beneath the nipple).

Ulceration.—Not recorded except as an ulcerated recurrent nodule in the case of the patient who a year previously had had a "large" growth removed; this had been noticed for the first time only 2 months previous to first admission and operation, and was therefore probably of rapid growth.

Size.—In the case just mentioned the growth was "large"; in 2 others it was "small."

De Morgan's Spots.—These are recorded as present in 1 of the 4 cases.

Secondary Growths.—Three cases showed enlargement of the axillary glands.

Clinical Observations.—*Age.*—The ages of the patients were respectively 53 (on admission to the Hospital in 1903), 29, 70, and 56, giving a mean age of 52 years.

Occupation.—The occupations of the patients were, in the same order as that just given, those of porter, cabman, optician, and stationer respectively.

Family history of tuberculosis or malignant disease.—None recorded.

History of previous injuries.—None recorded.

Pain.—Absent in the first 2 cases; some pain associated with the recurrence in the scar in the third; "tenderness" only mentioned in the fourth.

First manifestation of the disease.—A "lump" in the first two cases; not recorded in the third; tenderness on pressure in the fourth.

General health and emaciation.—In the same order as before, the patients were "emaciated," "fairly well nourished," "well nourished," and "well nourished" on admission.

Duration.—On admission to the Hospital the disease had lasted, according to the patients' own accounts, 2, 3, 195, and 12 months respectively.

V. SARCOMA OF THE BREAST.

Eleven cases of sarcoma of the breast are recorded during the five years 1904–1908; 9 were primary and 2 secondary, all in females.

Side Affected.—The left breast was the site of primary sarcoma in 5, the right in 4, instances; in none of these was the opposite breast invaded by new growth.

Site of Primary Growth.—This is stated in 6 of the 9 cases:—

Upper and outer quadrant . . .	2 cases
Upper and inner ,, . . .	1 case
Lower part of breast	1 ,,
Outer ,, ,, ...	1 ,,
Beneath nipple (central)	1 ,,

These figures, though small, agree with those of the earlier paper in indicating that sarcoma tends to originate chiefly in the upper and outer parts of the breast, as is the case with carcinoma.

Retraction of the Nipple.—Present in 2 cases, absent in 2 cases; not mentioned in the remaining 5. The percentage of cases of retraction of the nipple, 22·2, agrees closely with the 18·2 of the previous paper.

Size.—The growth was "large" in all 6 cases in which the size "on admission" is mentioned. This observation agrees with those recorded in the earlier paper.

Histological Varieties.—These were as follows:—Small round-cell, 4; spindle-cell, 2 (one of these doubtfully included under this heading); mixed-cell, 3.

Œdema of the Arm.—This is recorded as present in 1 case only, at about the end of the 5th year.

Secondary Growths.—The present series includes only 2 post-mortem examinations. In one the sarcoma was found to extend to the axilla, ribs, and lung, no further deposits being found; in the other case secondary growths were found in liver, pancreas, kidney, adrenal, peritoneum, pericardium, lung, and thyroid, and in lumbar, mesenteric, cervical, supraclavicular, and axillary glands.

Clinical Observations.—*Age.*—The ages at onset in the 9 cases at present under consideration ranged from 51 to 88 years, with an average age at onset of 65·6 years, that found in the previous paper in 41 cases being 45·5 years. This paragraph and the next following illustrate well the need for large figures in making statistical observations.

Civil state.—All of the 9 patients with 1 exception were married. In 2 cases the number of children is not given: the remaining 6 patients had among them 55 children—an average of over 9. The suggestion here that sarcoma is twice as common in married women as in unmarried is diametrically opposed to that raised in the earlier article, viz., that sarcoma is twice as common in single women as in married; that suggestion, however, has the advantage of being based on 39 cases.

Occupation.—Housework in all 9 cases.

Lactation.—Information is given in the notes in 5 cases as follows:—"Nursed all 8 children"; "All 13 breast-fed"; "Nursed all 10 children"; "Suckled all 9 children with left breast" (the growth was situated in this breast); "None of the 11 children breast-fed except the first."

History.—A family history of tuberculosis is given in 3 cases, and of malignant disease in 1. No history of personal injury is recorded in any of the 9 cases.

Pain.—In 8 of the 9 cases pain was stated to be present, although only to a slight extent in 3 of these. In the remaining 1 case it was absent.

Ulceration.—This is recorded in 5 of the 9 cases. In 2 of these instances its date of appearance is given, viz., 12 and 15 months respectively after that of the first sign of the disease.

Emaciation.—One patient was emaciated on admission, two fairly well nourished, four well-nourished. For all nine the average duration of disease before admission was 21 months.

Secondary Sarcoma of the Breast.—Two cases are reported; in each the primary growth was melanotic sarcoma of the skin. In one of these the heel was the seat of the primary growth, and both breasts were invaded by secondary deposits; in the other the primary growth occurred in the skin of the thigh, and the right breast was secondarily involved.

VI. THE HISTOLOGY OF MALIGNANT GROWTHS OF THE BREAST IN GENERAL.

In the present investigation a microscopic diagnosis of malignant disease has been made in 380 cases. Care has been taken that no case should be counted more than once through having been made, on account of recurrence, etc., the subject of several microscopic examinations. Although the histological side of the cases of the year 1904 was dealt with in the earlier research, which in every other respect was carried up to the end only of the year 1903, these cases are included here also for the sake of completeness, so that overlapping occurs to some extent.

It is to be noted that a small number of cases in which breasts removed for malignant disease at private operations were submitted to the Cancer Research Laboratories for microscopical examination, and which do not otherwise affect the present investigation, are here included.

Histological Varieties of Growth.—The 380 cases are subdivided and arranged in tabular form as follows:—

TABLE X.

Table showing the Numbers of the Different Histological Varieties of Malignant Disease of the Breast microscopically examined during the five years 1904–1908.

Year ...	1904	1905	1906	1907	1908	Total.
Spheroidal-cell carcinoma	63	39	56	49	66	273
Columnar-cell carcinoma	3	3	6	6	2	20
Sarcoma	2	2	4	1	2	11
Endothelioma	7	4	4	9	8	32
Histology doubtful ...	2	9	11	13	8	43
Endothelioma and Sph. carcinoma	—	—	—	—	1	1
Total	77	57	81	78	87	380

The cases placed in the above table under the heading "Histology doubtful" are almost entirely cases in which the microscopic diagnosis lay between endothelioma and spheroidal-cell carcinoma, and would therefore by most histologists have been placed in the last-mentioned group.

The numbers and percentages of the different histological varieties for the whole period of 5 years, 1904–1908, are given in the following table and compared with those found in the previous investigation; the figures for the whole period of 9 years, 1900–1908, dealt with in the two papers together may be conveniently given at the same time:—

TABLE XI.

Table showing the Numbers and Percentages of the different Histological Varieties of Malignant Disease of the Breast microscopically examined during the Periods mentioned below.

Period ...	1904–1908.		1900–1904.		1900–1908.	
Spheroidal-cell carcinoma	273	71·8	233	77·7	442	73·3
Columnar-cell carcinoma	20	5·3	12	4·0	29	4·8
Sarcoma	11	2·9	23	7·7	32	5·3
Endothelioma	32	8·4	32	10·6	56	9·3
Histology doubtful	43	11·3	—	—	43	7·1
Endothelioma and Sph. carcinoma ...	1	0·3	—	—	1	0·2
	380	100·0	300	100·0	603	100·0

Allowing for the fact that the cases of doubtful histology must be divided almost entirely between the spheroidal-cell carcinomata and the endotheliomata, it is seen that the only considerable relative difference between the various columns in the foregoing table occurs in the case of the sarcomata; for this discrepancy the comparative smallness of the numbers dealt with must be held responsible. On the whole, it may with a fair amount of probability be inferred that spheroidal-cell carcinomata form rather more than three-fourths of all malignant growths of the breast, and with endotheliomata make up about 90 per cent. of all cases, the remaining 10 per cent. being divided nearly equally between sarcomata and columnar-cell carcinomata.

On reviewing this paper as a whole it is seen that a general agreement between the results of the present investigation and those found in the previous research has been well maintained, and it may be stated broadly that considerable relative differences have been observed only in those cases in which they might reasonably have been expected, viz., those in which only small numbers have been available.

A CONTRIBUTION TO THE STUDY OF EREPSIN IN MALIGNANT DISEASE.

By HECTOR A. COLWELL.

Introductory.—In 1901 O. Cohnheim (1) showed that the mucosa of the small intestine of the dog contains a peptone-splitting enzyme which he termed "Erepsin." This enzyme has been made the subject of numerous researches by Vernon (2), who demonstrated its presence in all animal tissues which he examined, whether those of vertebrates or invertebrates. Generally, it may be said that the tissues of the higher members of the animal kingdom contain more than those of the lower, and those of healthy animals than corresponding tissues of diseased animals of the same species. The ferment acts best at a temperature of about 37° C. (3) (even when derived from a cold-blooded animal) and in a faintly alkaline medium. A ·1% solution of sodium carbonate was found to be the most suitable. Stronger concentrations have a powerfully destructive effect upon erepsin as upon many other enzymes. Exposure to X-rays or radium (4) is stated not to affect erepsin, though it is powerfully destructive to ptyalin, pepsin, trypsin, and pancreatic diastase (5). This I have confirmed. Firstly, by exposing four active tissue extracts to the X-rays for two hours daily on six consecutive days: the ereptic power was in each case identical with that of an unexposed control. Similarly, another extract was exposed to the action of 5 mgr. of radium bromide for 72 hours continuously: after a portion had been removed for examination, the remainder was re-exposed for another four days. Neither exposed sample differed in power from the control.

Scope of Present Enquiry.—The experiments described in this paper were undertaken in order to ascertain what difference, if any, exists between the ereptic power of the tissues of patients who had died from malignant disease, and those dying from other causes.

The tissues examined were, the kidney (in all cases), the liver and spleen in the majority of cases, and where practicable the new growth.

Method of experiment.—The materials were obtained as fresh as possible from the post-mortem room, roughly freed from blood or other extraneous tissue, and finely minced. To each gram of the minced material were added 2 cc. of pure glycerin, the mixtures being preserved in stoppered bottles at the ordinary room temperature for 21 days. Each bottle was shaken once a day. At the end of the 21 days the glycerin extract was filtered through glass wool, and its peptone-splitting power observed in the following manner. A 2·5% solution of Witte peptone in ·1% sodium carbonate was made by adding filtered 5% solution of Witte peptone to an equal volume of ·2% sodium carbonate.* To 20 cc. of this dilute alkaline peptone solution was added ·5 cc. of the extract under examination and a few drops of toluol as a preservative. This mixture, contained in a small stoppered bottle, was placed in the incubator at 37° C. for 24 hours, and the relative amount of peptone split up by the extract determined by the method employed by Vernon in his investigations. It consists in an application of the "biuret" reaction for proteids; and its applicability depends upon the fact that it is only given by protein bodies and not by the decomposition products which are formed by the action of erepsin. Two Nessler glasses are taken, and into each are run 2 cc. of a centi-normal solution of copper sulphate, and 20 cc. of a normal solution of sodium hydrate. To the first tube, which is to serve as the control, is added ·5 cc. of the 2·5% control solution of Witte peptone. To the second tube the partially digested peptone solution is added till the tints in the two tubes, when examined by transmitted light, are identical. Since only the undecomposed peptone gives the characteristic colour with copper sulphate and sodium hydrate, it follows that when sufficient partially digested peptone has been added to give the same tint as the control, the quantities of undecomposed peptone added to the experimental and control tubes are identical.

In this connection three practical points may be noted:

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* The ·2 per cent. sodium carbonate must be prepared in bulk, inasmuch as slight variations in alkalinity profoundly alter the reaction.

(1) If a layer of bubbles be formed on the surface of the fluids they may be caused to disappear by allowing a small quantity of ether vapour to fall upon them ; (2) When making an observation, if too much peptone be added, the resulting tint may appear paler than the control and of a peculiar yellowish pink colour ; (3) As Vernon has pointed out, the tint requires an appreciable time for its development. When undigested peptone is used, the tint reaches about 93% of its maximum in one minute ; with partially decomposed peptone the rate is considerably more rapid.

From what has been said it will be seen that the greater the ereptic power of an extract which is employed in any given digestion, the greater will be the amount of peptone solution partially digested by it, which must be used to produce a tint equal in depth to the control tint. In the tables which follow are given the number of cc. of peptone, partly digested by an extract of the organ specified, which must be used to produce a tint similar to that produced by ·5 cc. of the control.

The tissues examined in the present research were derived from 80 autopsies performed at the Middlesex Hospital. Of these, 32 were upon cases of malignant disease, and 48 upon other cases. The 32 malignant cases are allotted as follows :—Breast 10, Uterus and Bladder 9, Alimentary system 7, and " other sites " 6. Of the 48 non-malignant cases, Bronchitis accounts for 7, Broncho-pneumonia 3, Pneumonia 3, Phthisis 4, Renal diseases 3, Diseases of the circulatory system 8, Septic troubles 5, Diseases of the digestive tract, liver, and pancreas 4, Delirium tremens 1, Diabetes 1, Hydrocephalus 1, Spina bifida 1, Suppurative arthritis 1, Asphyxia 2, Acute intestinal obstruction 3, and Fracture of the skull 1. This last was the only case in which all the organs were described as " normal."

RESULTS.

In all, 80 specimens of kidney were examined, 78 of liver, and 59 of spleen. Taking an average of all the cases examined, it is found that ·96 cc. of " kidney peptone," ·79 cc. of " liver peptone," and ·73 cc. of " spleen peptone " * are required to give the same tint as ·5 cc. of the control.

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* Peptone partially digested by the action of kidney, &c., extract.

In the non-malignant series of cases, 48 specimens of kidney, 47 of liver, and 33 of spleen were examined. Here it was found that ·95 cc. of "kidney peptone," ·79 of "liver peptone," and ·73 cc. of "spleen peptone" were required to produce the same result.

In the malignant series, 32 specimens of kidney were examined, 31 of liver, and 26 of spleen. The corresponding values for the glycerin extracts are ·96 cc. for kidney, ·80 for liver, and ·74 for spleen. These figures, being in both cases averages of a series composed of widely varying elements, may be taken as practically identical.

If, however, the following series of 15 cases be considered, the result will be found to be somewhat different. The cases selected are those between the ages of 12 and 65, which either died from accident, some acute disease, or from bronchitis, and which were not the subject of operation for disease of long standing.

TABLE I.

Showing the amount (in cc.) of Peptone digested with Kidney, Liver or Spleen Extract, which must be used to give a Tint equal to ·5 cc. of undigested Peptone.

—	Disease.	Sex.	Age.	Kidney.	Liver.	Spleen.
1	Fractured skull	M	40	·95	·84	·75
2	Death under anaesthetic (suppurative arthritis)	F	12	1·05	·82	·75
3	Bronchitis	F	50	·99	·90	·80
4	"	M	63	1·35	·90	·80
5	"	M	57	·96	·77	·72
6	"	M	52	·96	·86	·74
7	"	M	58	·98	·82	—
8	"	M	37	·90	·74	—
9	Pneumonia	M	42	·95	·87	·72
10	"	M	24	1·30	1·10	·80
11	"	F	26	·90	·75	—
12	Heart failure	F	50	1·05	·87	·75
13	Infective endocarditis	M	44	·95	·74	—
14	Intestinal obstruction	F	59	1·10	·85	—
15	Delirium tremens	M	54	1·50	·75	—
	Average	—	—	1·06	·84	·76

Strictly speaking, the mean values in Table I are those for otherwise healthy persons who died after a short illness.

They may probably be regarded as "normal," since Vernon (2) has shown that the tissues of guinea-pigs undergo no change in ereptic power as the result of short illnesses, even though acute. Comparing them with the means for *all* non-malignant and malignant cases, it is seen that the values for these latter, in the case of the kidney at least, are distinctly lower.

TABLE II.

To show the difference in Ereptic Power between Tissue Extracts obtained from all Malignant and Non-Malignant cases and Normal Extracts.

—	Kidney.	Liver.	Spleen.
Means of normal extracts	1·06	·84	·76
„ „ all non-malignant cases	·95	·79	·73
„ „ malignant cases	·96	·80	·74

Chronic disease of an organ, such as interstitial nephritis or cirrhosis of the liver, always appears to lead to a diminution in its ereptic power. In some cases, however, unexpected values are obtained for macroscopically normal organs, for which no good reason can be assigned.

From Table V, in which the average figures for different groups of malignant cases are given, and Table IV, in which the details of individual cases are given, the following facts may be deduced. In cases of cancer of the breast, the average figure for kidney is as high as in the selected control, that for liver somewhat lower, and that for spleen practically identical. On reference to Table IV it will be seen that for the kidney, 3 cases show a value well above the control, 3 are approximately equal to it, and 4 definitely below. Thus of the 10 cases of breast cancer, 7 are either equal to or below the control, and the very high figure is due to the high figure obtained in 3 individual cases. In the case of the liver (from the same series of cases) only 1 is above the average, 5 are the same, and 1 below; and in the case of the spleen 1 is above, 8 the same, and 1 below.

TABLE III.

Ereptic Power of Tissues in Non-Malignant cases.

—	Nature of Disease.	Sex.	Age.	Kidney.	Liver.	Spleen.
1	Suppurative arthritis (death under anæsthetic)	F	12	1·05	·82	·75
2	Broncho-pneumonia	F	3/12	·89	·66	·84
3	,, ,,	F	9/12	·90	·79	·72
4	,, ,,	F	14/12	·80	·65	—
5	Bronchitis	F	50	·99	·68	·64
6	,,	M	63	1·35	·90	·80
7	,,	M	57	·96	·77	·72
8	,,	M	52	·96	·86	·74
9	,,	M	58	·98	·82	—
10	,,	M	37	·90	·74	—
11	,,	M	85	·90	·75	·73
12	Pneumonia	M	42	·95	·87	·72
13	,,	M	24	1·30	1·10	·80
14	,,	F	26	·90	·75	—
15	Phthisis	F	16	·99	·84	·70
16	,,	F	23	·97	·79	·75
17	,,	F	27	·72	·70	·70
18	,,	F	17	·88	·72	·68
19	Asphyxia (some chronic int. nephritis)	M	50	·96	·89	·71
20	Asphyxia	M	4/12	·96	·80	—
21	Heart failure (chr. myocarditis)	F	50	1·05	·87	·75
22	Morbus cordis	F	62	·72	·59	—
23	,, ,,	M	51	·90	·75	—
24	,, ,,	M	56	·89	·84	—
25	,, ,,	M	34	·85	·75	·65
26	Mitral stenosis	M	34	·92	·81	·74
27	Raynaud's disease	F	53	·84	·78	·73
28	Morbus cordis	M	51	·91	·78	·68
29	General peritonitis	F	25	·91	·72	·65
30	Pyosalpinx	F	39	·89	·84	·80
31	Infective endocarditis	M	44	·95	·68	·73
32	Septicæmia	M	52	·95	·74	—
33	Pyosalpinx	F	37	·97	·75	—
34	Volvulus	M	71	·81	·90	·73
35	Strangulated hernia	M	67	·80	·80	·75
36	Cirrhosis of liver	M	47	·93	·65	·68
37	Gastric ulcer (perforation)	F	39	·95	·83	—
38	Ulcerative colitis	F	46	·85	·78	—
39	Acute intestinal obstruction	F	59	1·10	·85	—
40	Chronic pancreatitis	M	50	1·6	1·00	·75
41	Delirium tremens	M	54	1·5	·75	·76
42	Diabetes	M	66	·86	—	—
43	Hydrocephalus	M	17/12	·71	·67	—
44	Spina bifida	M	2/365	·80	·70	·68
45	Fractured skull	M	40	·95	·84	·75
46	Pyelonephritis	F	38	1·20	·94	·75
47	Chronic interstitial nephritis (early)	M	52	·86	·77	·72
48	Chronic interstitial nephritis (early)	M	71	·87	·97	·80
	Average of all non-malignant cases	—	—	·95	·79	·73

TABLE IV.

Ereptic Power of Tissues in Malignant cases.

—	Site.	Sex.	Age.	Kidney.	Liver.	Spleen.	Growth.
1	Breast	F	45	1·20	·75	·74	—
2	,, ...	F	61	1·40	·80	·84	—
3	,, ...	F	48	1·20	·90	·60	·70
4	,, ...	F	47	1·00	·84	·80	—
5	,, ...	F	57	·95	·75	·80	—
6	,, ...	F	61	1·00	·75	·76	—
7	,, ...	F	56	·91	·80	·74	—
8	,, ...	F	54	1·10	·80	·70	—
9	,, ...	F	45	·95	·80	·75	·68
10	,, ...	F	37	·95	·76	·73	—
11	Bladder	F	70	·70	·75	·70	—
12	Cervix uteri	F	54	·76	·87	·60	—
13	Uterus (sarcoma)	F	17	1·20	·86	·79	·75
14	Cervix uteri	F	33	·95	·90	·75	—
15	,, ,, ...	F	59	·71	·65	·72	—
16	,, ,, ...	F	60	·75	·67	—	—
17	,, ,, ...	F	52	·96	·85	—	—
18	,, ,, ...	F	49	·98	·78	—	—
19	,, ,, ...	F	48	·85	·69	·66	—
20	Tongue	M	43	1·20	1·00	1·00	·70
21	Mouth	M	60	·71	·68	·69	—
22	Stomach	M	53	·87	·75	·65	—
23	Colon	F	60	·75	·80	·70	—
24	Rectum	M	65	1·00	·82	—	—
25	Parotid	M	71	·96	·72	·72	·70
26	Pancreas	F	57	1·40	1·00	·80	—
27	Face...	F	73	1·00	·80	·90	·75
28	Larynx	M	32	·90	·83	·72	—
29	Skin (melanotic sarcoma)	M	68	1·00	·90	·80	·75
30	Face...	M	70	·84	·75	·70	—
31	Adrenal	F	38	·75	—	—	—
32	Peritoneum (Colloid) ...	F	57	·90	·76	—	·65
	Average of all malignant cases	—	—	·96	·80	·74	·71

TABLE V.

To show the Comparative Values obtained for the different series of Malignant cases examined.

—	Kidney.	Liver.	Spleen.
Normal means (Table I)	1·06	·84	·76
Means of all malignant cases	·96	·80	·74
,, ,, cases of breast cancer	1·06	·79	·75
,, ,, cases of uterus and bladder cancer ...	·87	·78	·70
,, ,, cases of cancer of alimentary system ...	·98	·82	·65
,, ,, remaining malignant cases	·90	·81	·78

From this it appears that the ereptic power of the tissues in malignant disease is below the normal, whatever the site of the primary growth. The low value obtained for kidney in cancer of the uterus and bladder is, at any rate, partly due to the secondary renal changes so frequently accompanying disease in these regions. The very high values obtained for kidney in three cases of breast are inexplicable; in particular they cannot be explained on the generally accepted view that a fall in ereptic power goes hand in hand with bodily malnutrition, since two of the cases in question were emaciated.

In eight cases samples of the growth were obtained (cf. Table IV). The average is lower than the average values for kidney, liver, or spleen; and in all cases except one (No. 2) it was the lowest value obtained for any tissue in the given case.

To sum up. My observations confirm the view that the ereptic values of tissues from cases which are the subject of serious and chronic organic disease tend to be lower than normal. They add the further fact that malignant disease, as a whole, conforms to this rule, while the values obtained are neither higher nor lower than those met with in other chronic morbid conditions.

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(3) Vernon, "Journ. Physiology," xxx, p. 330 et seq.
(4) Neuberg, "Berlin Klin. Wochenschr.," xli, 1081.
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PRELIMINARY NOTE ON THE EREPTIC POWER OF THE TISSUES OF NORMAL AND CANCEROUS MICE.

By H. A. COLWELL and H. MacCORMAC.

In the present number of the Archives a paper appears by one of us dealing with the ereptic values of human tissues under various conditions. As some estimations of this ferment in cancerous mice were being made by us we have ventured to give our result, so far obtained, in this note.

Of the mice used, into some—the "cancerous mice"—an inoculation with Jensen's tumour had been practised, and had grown. We are indebted to the kindness of Dr. Bashford for this tumour. Controls were selected from normal mice, as nearly as possible of the same age and size as the cancerous.

At first trial we used 4 cancerous and 3 normals. In the former the tumours were well grown, but there was no ulceration nor were the tumours very necrotic. The animals seemed but little disturbed in their general health.

The animals having been killed with chloroform, the tumours and certain other parts were taken; a list of these is given later. Each selected tissue was minced as finely as possible and extracted in 40 per cent. spirit for seven days; this was then filtered, and the filtrate allowed to act upon peptone and the amount of peptone-splitting estimated: details of this process have been fully given in the previous paper already referred to.

TABLE I.

Showing the number of cubic centimetres used to match ·5 c.c. control peptone solution.

—	Cancerous Mice.					Normal Mice.			
	1.	2.	3.	4.	Average.	1.	2.	3.	Average.
Tumour	·6	·7	·6	·7	·65	—	—	—	—
Spleen	·6	·7	·65	—	·65	·55	—	—	·55
Liver	·7	·6	·6	·7	·65	—	·5	·7	·6
Kidney	·7	·8	·7	·7	·73	—	·6	·6	·6
Lung	—	—	·6	—	·6	·7	·6	·6	·63

In the above table it will be seen that several times no estimation has been made for a certain organ. Where such is the case the material had not been sufficient to give values which could be regarded as reliable.

In order to avoid such a difficulty, two sets of three mice, one set of cancerous and the other of normals, were taken. Similar tissues from each set were pooled, thereby giving larger working quantities. These tissues were extracted in 70 per cent. glycerine and estimated, the methods being exactly the same as that already described (p. 97).

The findings are as follows :—

TABLE II.

Showing the number of cubic centimetres required to match ·5 c.c. control peptone solution.

—	Cancerous Mice.	Normal Mice.
Tumour	·6	—
Brain	·55	·55
Spleen	·6	·55
Liver	·6	·6
Kidney	·7	·65
Heart	·6	·55
Lungs	·6	—

An examination of these tables suggests that there tends to be a very slightly higher ereptic value for the tissues of mice harbouring a tumour than in the normals. This is borne out by both alcohol- and glycerine-extracted material.

Sufficient trials have not yet been made to draw definite conclusions, for it has been shown by Vernon and others that individual ereptic variations are considerable.

They offer a contrast to that which one of us has found in malignant disease of the human subject, and in this respect agree with the observations of Copeman and Hake upon the secretion of gastric hydrochloric acid by cancerous mice. On the other hand, it must be conceded that diminished ereptic power of the tissues goes hand in hand with chronic disease and emaciation, and that the animals used in the present research, although forming considerable growths, appeared to be in good health.

A METHOD OF QUANTITATIVE ANALYSIS OF THE TISSUES FOR POTASSIUM AND SODIUM BY MEANS OF THE SPECTROSCOPE.

By J. C. MOTTRAM.

Previous Work.—The chemist has chiefly used the spectroscope for qualitative analysis, and especially in those cases to which the usual chemical methods cannot be applied. Many of the early workers with the spectroscope used it for quantitative analysis, but no records have been found of any recent researches in this direction. Quantitative estimations were made by Miller (1862) of an alloy, by Champion Pillet and Grenier of alkalis, Lockyer and Robert Austen (1870) of alloys of gold and silver, lead and cadmium; the latter authors used a photographic method depending on the fact that the length of the line in the spectrum varies directly with the percentage of the metal in the alloy. Sir J. C. Alleyne quantitatively estimated the phosphorus in iron and steel, Liveing and Dewar, the amount of sodium by measuring the width of the sodium lines; Hartley, copper in pyrites cinder, lead, silver, and copper in zinc blende, by comparing the ultra-violet photographic spectra of solutions of the different elements in varying strength. In 1877 Swan found that the smallest amount of sodium recognisable by the spectroscope is $\frac{1}{2,500,000}$ grain; the following is a sample of the results obtained by Kirchoff and Bunsen and other workers as regards the least amounts that can be seen with the spectroscope:—

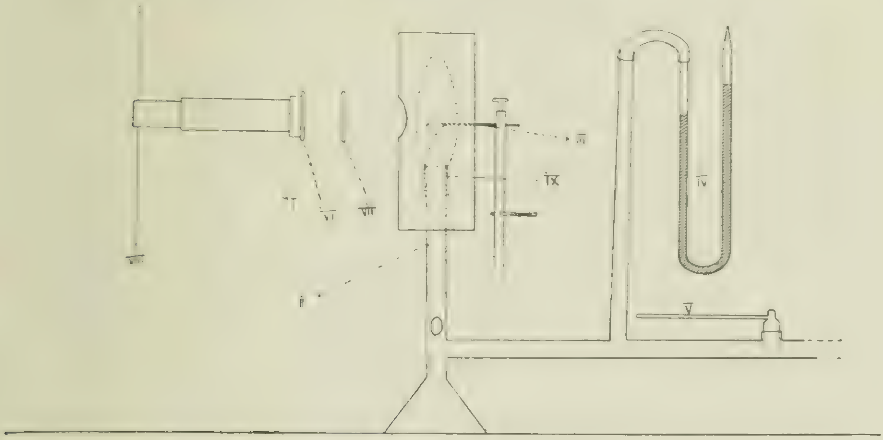
	Flame Spectra.	Spark Spectra.
Calcium	$\frac{1}{50,000}$ mgr.	$\frac{1}{10,000,000}$ mgr.
Lithium	$\frac{1}{600,000}$ mgr.	$\frac{1}{40,000,000}$ mgr.
Potassium	$\frac{1}{3,000}$ mgr.	$\frac{1}{400}$ mgr.
Sodium	$\frac{1}{14,000,000}$ mgr.	

(From Watt's Dictionary of Chemistry, Article "The Spectroscope.")

H. Bullman used the spectroscope for the quantitative estimation of lithium; he found that if a solution of lithium chloride be diluted until the Li_a line disappears there is then contained in every 3345 cc. of the solution 1·0 mgr. of the salt ("Zeitschr. Anal. Chem." xiv, 297–301, from extracts of the Chemical Society). Bullman's method differs from that to be described chiefly in the fact that the solution was introduced into the flame upon a cylindrical spiral of platinum after being dried by approximation to the flame.

Absorption spectra have been utilised for quantitative estimations by finding the strength of a solution which will just give the absorption lines of the metal being estimated.

Owing to the easier volatility of the chlorides of metals this salt has been employed largely, but for reasons to be given later chlorides are inadmissible in the present research, and have therefore been replaced by sulphates.



The Method.

1. **The Apparatus.**—

   i. A Direct Vision Spectroscope with a fixed slit; one was chosen through which a faint band could be best seen.

   ii. A Bunsen burner guarded with a blackened metal cylinder having a hole on one side through which to view the flame, and a slit through which to introduce the platinum spoon.

iii. A platinum spoon capable of holding from 1 to 1·5 cc.
iv. A toluol manometer for measuring the gas pressure.
v. A gas tap with a long arm for delicate adjustments.
vi. A cobalt glass fixed to the front of the spectroscope.
vii. A loose cobalt glass to be placed between the flame and the spectroscope when required.

Note.—Nos. vi and vii are for the purpose of obtaining a sodium-free spectrum.

viii. A paper screen to protect the eyes from the light of the flame.
ix. A platinum gauze nozzle fixed to the top of the Bunsen burner.

Besides which are required :—

i. Several pipettes graduated to deliver 0·02 cc.
ii. Pure sulphuric acid.
iii. Distilled water.

Note.—Both of these were potassium free and as nearly sodium free as could be obtained.

2. **Precautions.**—The observations must be taken under identical conditions. The following is a list of those found necessary :—

i. The distance from the cobalt glass fixed in front of the spectroscope to the metal cylinder guarding the flame must always be the same (in these experiments 3·7 centimetres).
ii. The position of the spoon in the flame must be constant. In these experiments it was so placed that the bottom of the spoon was just above the apex of the blue inner zone of the flame when the spoon was hot, but not in contact with it.
iii. The gas pressure must be constant as measured by the difference in heights of the toluol in the manometer (in these experiments ·3 centimetres).
iv. The amount of diffuse light in the room must be small and constant (in these experiments daylight was excluded and replaced by an eight-candle-power electric lamp).

v. The spectroscope must have a fixed slit.

vi. The spectroscope must always be directed to the same part of the flame; it was directed above the spoon so that the continuous spectrum produced by the incandescent spoon was just invisible.

vii. The first definitive observations were postponed until the eyes had become accustomed to the dull light of the room (about half an hour).

3. **The actual Steps of the Analysis.**—Before describing the method of making the analysis, it is necessary to point out that (1) the time taken by a salt to vaporise as estimated by the length of time the spectrum of the metal can be seen is proportional to the amount of salt placed on the spoon; that (2) the presence of another metallic salt or of carbon influences the rate of vaporisation; that (3) the rate of vaporisation varies with the acid radicles forming the salts, the metals themselves being constant. Each of these factors is considered later, and in the method of analysis now to be described all have been taken into account.

About 0·1 grm. of the tissue to be examined is introduced into a clean dry test-tube and weighed to four decimal places; a few cubic centimetres of strong sulphuric acid are added, and the whole heated until the tissue is completely broken up and a clear dark liquid results; this is allowed to cool, and then is made up to 5 cc. with strong sulphuric acid.

A. *Estimation of Sodium.*—The method depends on the fact that different quantities of sodium sulphate, when placed on the spoon and introduced into the flame, take different lengths of time to burn off. The time is proportional to the amount.

Having cleaned the platinum spoon with strong hydrochloric acid and a blowpipe until the D line can no longer be seen through the *two* cobalt glasses, 0·02 cc. of the above dark liquid is placed in the spoon and the sulphuric acid evaporated off without ebullition by approximating it to the flame. When dry the bottom and sides of the spoon will be found to be covered with a thin film of carbon; by momentarily introducing the spoon into the flame (until the spoon just glows) this is instantly burnt off. As is shown later, no sodium is lost during this operation. Next a drop of strong sulphuric acid is added to make sure that the sodium is all in the form of sulphate; the sulphuric acid is evaporated off as before, and the spoon then definitively introduced into the flame. Examinations through the spectroscope and the *two* cobalt glasses are made at intervals of half a minute; the D line of sodium, which at first is clearly seen, gradually becomes faint until a point is reached when it can no longer be seen; the time is then noted. The reading so obtained is compared with a table of readings previously formed when known weights of sodium were placed on the spoon, and from this the percentage of sodium in the tissues is estimated.

The following is a portion of a table so made:—

6½	minutes	corresponds	to	·000001	grms.	of sodium.
7	,,	,,	,,	·00000114	,,	,,
7½	,,	,,	,,	·00000128	,,	,,
8	,,	,,	,,	·00000143	,,	,,
8½	,,	,,	,,	·00000157	,,	,,
9	,,	,,	,,	·00000172	,,	,,
9½	,,	,,	,,	·00000186	,,	,,
10	,,	,,	,,	·000002	,,	,,
10½	,,	,,	,,	·00000216	,,	,,
11	,,	,,	,,	·00000233	,,	,,
11½	,,	,,	,,	·00000250	,,	,,
12	,,	,,	,,	·00000267	,,	,,
12½	,,	,,	,,	·00000284	,,	,,
13	,,	,,	,,	·000003	,,	,,

Example.—Liver dried and extracted with ether; 0·1880 grms. taken and made up to 5 cc. with strong sulphuric acid—

0·02 cc. of this gave a reading of 8 minutes.
0·04 cc. ,, ,, ,, 13 ,,

Referring to the table above,

8 minutes corresponds to ·0000143 grms.
13 ,, ,, ·000003 ,,

Therefore in ·02 cc of the solution there are ·0000015 grms. of Na.

Therefore in 5 cc. or in ·1880 grms. liver there are $\frac{\cdot0000015 \times 5}{\cdot02}$ grms. of Na.

Therefore in 1000 grms. liver there are $\frac{\cdot0000015 \times 5 \times 1000}{\cdot02 \times \cdot1880}$ grms. of Na.

$$= \frac{750}{376} = 2 \text{ grms. of Na}$$
$$= 2 \text{ pts. of Na per } 1000.$$

B. *Estimation of Potassium.*—In this case the estimation depends upon the least amount of potassium as sulphate that will give the band A in the red ; this amount has been found to be with this apparatus ·0000002 grms.

In a clean test-tube is placed 0·5 cc. of the sulphuric acid solution mentioned above ; distilled water is gradually added, observations being made between each dilution in the following way :—0·02 cc. of the dilution is placed in the platinum spoon, evaporated to dryness by approximation to the flame ; a drop of strong sulphuric acid is then added to make certain that the potassium is in the form of sulphate and the excess of sulphuric acid evaporated off. The spoon is now placed in the flame and the red potassium band observed through the spectroscope and *one* cobalt glass ; if visible further dilution is necessary until the band becomes invisible, when the number of cc. of distilled water used when the potassium band was last seen is noted ; then every 0·02 cc. of this solution must contain ·0000002 grms. of potassium, and from this can be calculated the percentage of potassium in the tissue.

Example.—·1150 grms. of blood taken and made up to 5 cc. with strong sulphuric acid ; 0·5 cc. of this taken and diluted ; after the addition of 1·5 cc. water the red potassium band could be just seen ; the addition of another ·5 cc. rendered it invisible.

Then in 0·02 cc. of this solution there are ·0000002 grms. of potassium.

Therefore in 2 cc. of this solution, or in ·5 cc. of the original solution, there are $\frac{\cdot0000002 \times 2}{\cdot02}$ of potassium.

Therefore in 5 cc. of the original solution, or in ·1150 grms. of blood, there are $\frac{\cdot0000002 \times 2 \times 5}{\cdot02 \times \cdot5}$ grms. of potassium.

Therefore in 1000 grms. blood there are

$$\frac{\cdot 0000002 \times 2 \times 5 \times 1000}{\cdot 02 \times \cdot 5 \times \cdot 1150} \text{ grms. of potassium}$$

$$= \frac{200}{115} = 1{\cdot}7 \text{ grms. of potassium.}$$

Therefore blood contains 1·7 parts of potassium per thousand.

(Carl Schmidt gives 1·739. Bunge, "Pathological Chemistry.")

Below is given an example of a complete estimation of sodium and potassium in muscle.

Example.—Muscle, human pectoral, ·5241 grms. taken and made up to 4 cc. with strong H_2SO_4 (sol. A):—1 cc. of this taken and 3 cc. of distilled water added (NOTE.—Dilution is sometimes necessary if the tissue contains much sodium, or a large quantity of tissue is taken).

With	0·02 cc.	of this	the D line	was visible for	5	minutes.
,,	0·04 cc.	,,	,,	,,	6½	,,
,,	0·08 cc.	,,	,,	,,	9½	,,

Referring to the table (p. 110) 6½ min. = ·000001 grms., and 9½ = ·00000186; the latter corresponding to ·08 cc., ·04 cc. contains ·00000093; the mean of these two observations is therefore ·000001 grms. Na in ·04 cc.

Therefore in 4 cc. or 1 cc. of sol. A there are $\frac{\cdot 000001 \times 4}{\cdot 04}$ grms. Na.

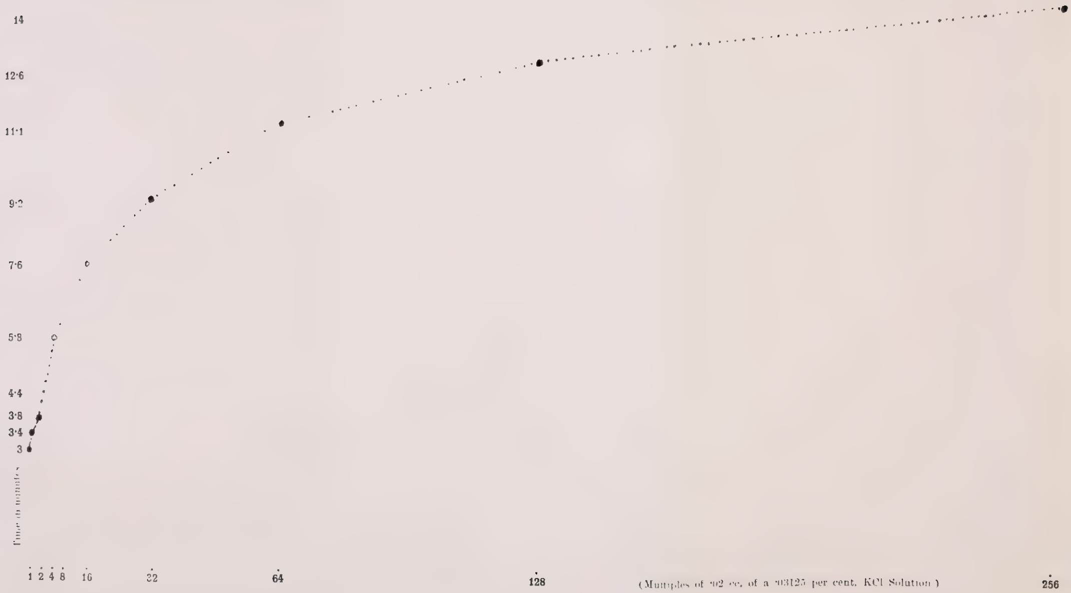
Therefore in 4 cc. of sol. A, or in ·5241 grms. muscle, there are $\frac{\cdot 000001 \times 4 \times 4}{\cdot 04}$ grms. Na.

Therefore in 1000 grms. muscle there are

$$\frac{\cdot 000001 \times 4 \times 4 \times 1000}{\cdot 04 \times \cdot 5241} = \cdot 76 \text{ grms. Na.}$$

Therefore muscle contains ·76 parts of sodium per thousand.

Estimation of Potassium.—0·5 cc. of the above sol. A taken and diluted with distilled water. When 18 cc. had been



THE QUANTITATIVE DETERMINATION OF POTASSIUM CHLORIDE WITH THE SPECTROSCOPE. SUCCESSION OF SINGLE DETERMINATIONS.

added 0·02 cc. just gave the red line. Then 0·02 cc. contains ·0000002 grms. of potassium.

Therefore 18·5 cc. or ·5 cc. of sol. A contains

$$\frac{\cdot0000002 \times 18\cdot5}{\cdot02} \text{ grms. of potassium.}$$

Therefore 4 cc. of sol. A, or ·5241 grms. muscle, contains

$$\frac{\cdot0000002 \times 18\cdot5 \times 4}{\cdot02 \times \cdot5} \text{ grms. of potassium.}$$

Therefore 1000 grms. of muscle contains

$$\frac{\cdot0000002 \times 18\cdot5 \times 4 \times 1000}{\cdot02 \times \cdot5 \times \cdot5241} \text{ grms. of potassium}$$

$$= 2\cdot8 \text{ grms. of potassium.}$$

Therefore muscle contains 2·8 parts of potassium per 1000.

J. Katz (from Schäfer's "Physiology") gives the following amounts in parts per thousand :—

Sodium - - - -	·3 — 1·5
Potassium - - -	2·4 — 4·6

The Rationale of the Method.

(i.) *The Estimation of Potassium in a Pure Solution of the Chloride.*

The original suggestion of Dr. Lazarus-Barlow that the potassium present in the tissues might be estimated by the length of time the red line A of potassium could be seen with a spectroscope was tested as a preliminary with pure potassium chloride; as is shown by the accompanying curve, a correlation obtains between the time taken for vaporisation and the amount of salt placed on the spoon. By this means the amount of potassium chloride in a solution can be estimated.

In the above curve the ordinates represent time in minutes, the abscissæ amounts of potassium chloride in multiples of ·02 cc. of a ·03125 per cent. solution. From this curve, having found the time, the amount of an unknown quantity of potassium chloride can be estimated by measurement; the extremities of the curve are not available: the end nearest the ordinate because very small amounts of potassium do not give the red line A, the other end because the addition of more potassium chloride causes only a small lengthening of the time.

(ii.) *The Estimation of Potassium as Chloride in a Mixture of two chemically pure Metallic Salts, whether Chlorides or other Acid Radicles be present.*

The effect of the presence of other metallic salts was then investigated, and it was found that they greatly alter the potassium rate of vaporisation, as is shown in the following table :—

	Mins.	Secs.
·02 cc. of 1 % KCl gave a potassium band visible for	4	0
·02 cc. of 1 % KCl + ·02 cc. of 1 % NaCl gave a potassium band visible for	0	35
·02 cc. of 1 % KCl + ·02 cc. of 8 % NaCl gave a potassium band visible for	0	30
·02 cc. of 1 % KCl + ·02 cc. of 1 % LiCl gave a potassium band visible for	0	75
·02 cc. of 1 % KCl + ·02 cc. of 8 % Na_2CO_3 gave a potassium band visible for	5	5
·02 cc. of 1 % KCl + ·02 cc. of very strong $CaCl_2$ gave a potassium band visible for	4	25
·02 cc. of 1 % KCl + ·02 cc. of a very strong $MgSO_4$ gave a potassium band visible for	6	75
·02 cc. of 1 % KCl + ·02 cc. of 1 % Na_2HPO_4 gave a potassium band visible for	10	75
·02 cc. of 1 % KCl + ·02 cc. of 8 % Na_2HPO_4 gave a potassium band visible for	22	0
·02 cc. of 1 % KCl + ·02 cc. of 8 % $FeSO_4$ gave a potassium band visible for	4	0

From this it appears that the greatest influence upon the rate of vaporisation of potassium chloride is produced by the salts of those metals, such as sodium and lithium, which give a flame spectrum, whereas metals giving no flame spectrum have little if any action. Of the same metal different salts produce different results : for instance, sodium chloride accelerates the vaporisation, sodium phosphate retards. Therefore in the presence of other metallic salts and other acid radicles the quantitative estimation of potassium cannot be carried out by this method ; subject to small differences the same was found to be true for sodium.

(iii.) *The Use of the Sulphates for Vaporisation—The Effect of Carbon.*

A. *Sodium.*—Since the animal tissues contain both sodium and potassium, it is clear from the above that no method of estimation of one metal by means of the spectroscope is available which leaves the other out of account. Hence search was made for salts which influence one another's rate of vaporisation as little as possible. The following table shows that this object is attained in the case of sodium by the use of the sulphates.

	Minutes.
·000001 grms. of sodium as sulphate rendered the D line visible for ...	6½
·000001 grms. of sodium as sulphate + ·000002 grms. of Potass. sulphate rendered the D line visible for	7
·000001 grms. of sodium as sulphate + ·0001 grms. of Potass. sulphate rendered the D line visible for	7¼
·000001 grms. of sodium as sulphate + very large quantity of $CaSO_4$ rendered the D line visible for...	6½
·000001 grms. of sodium as sulphate + very large quantity of $MgSO_4$ rendered the D line visible for	7

Thus the presence of 100 times as much potassium sulphate or an indefinitely large amount of calcium or magnesium sulphate makes a negligible difference in the rate of vaporisation. Hence it follows that the small amounts of potassium, calcium, and other metallic salts found associated with sodium in the tissues do not affect the sodium rate of vaporisation *when all are in the form of sulphates.*

Carbon was found to hasten the sodium rate of vaporisation, and this not from the presence of carbon *per se*, but because sodium sulphate is converted into sulphide and sulphite when heated with carbon. However, this difficulty can be overcome by oxidising the carbon by momentarily raising the spoon to a dull red heat in the flame; the subsequent addition of a drop of sulphuric acid ensures that all the salts are converted into sulphates. The following readings show that no sodium is lost in the process:—

·000001 grms. sodium as sulphate gave the D line visible for 6½ minutes.

·000001 grms. sodium as sulphate + small quantity of lamp black gave the D line visible 4½ minutes.

·000001 grms. sodium as sulphate + small quantity of lamp black (the carbon being first burnt off and then more sulphuric acid added) gave the D line visible 6¼, 6½, 6¼, 6¼ minutes in consecutive experiments.

B. Potassium.—Although potassium sulphate has little or no influence upon the rate of vaporisation of sodium sulphate, the converse is not the case. Hence the potassium can only be estimated by some other method. Experiments were therefore made to discover the smallest amount of potassium as sulphate that would give a visible band in the red; this was found to be ·0000002 grms. K. The amount ·000000185 could sometimes be seen, but more often not; the admixture of carbon, sulphate of sodium, calcium, or magnesium made no difference to this observation unless they were present in overwhelming amount (5000 : 1) as shown below:—

·0000002 grms. potassium as sulphate gave a visible potassium band.

·0000002 grms. potassium as sulphate + ·0001 grms. sodium as sulphate gave a visible potassium band.

·00000018 grms. potassium as sulphate + ·0001 grms. sodium as sulphate gave no potassium band.

·0000002 grms. potassium as sulphate + large quantity of carbon gave a visible potassium band.

·000000185 grms. potassium as sulphate + large quantity of carbon. potassium band sometimes seen.

·00000016 grms. potassium as sulphate + large quantity of carbon. potassium band never seen.

NOTE.—Unfortunately this method, depending upon the smallest amount that can be seen, could not be applied to sodium, because distilled water and strong sulphuric acid could not be obtained absolutely sodium-free.

The Error of the Method.

(i.) *Sodium.*—To estimate the range of error ten consecutive observations were made with ·000001 grms. of sodium as sulphate, and the following readings were obtained—$6\frac{1}{4}$, $6\frac{1}{4}$, $6\frac{3}{4}$, $6\frac{1}{2}$, $6\frac{1}{2}$, $6\frac{1}{2}$, $6\frac{1}{2}$. 7, $6\frac{1}{4}$, $6\frac{1}{4}$ minutes. The mean of the above is 6·475 minutes, and the difference between the greatest and smallest ·75 minutes, which is equivalent to a range of 11·5 per cent.

(ii.) *Potassium.*—In this case ·001 grms. of potassium as sulphate was diluted ten consecutive times with distilled water, 0·2 cc. being added at a time until the amount of potassium in 0·02 cc. was just sufficient to give the red line A. The following amounts were required:—9·8, 10·0, 9·6, 9·8, 10·0, 10·2, 9·6, 9·8, 10·0, 9·6 cubic centimetres; the mean is 9·84 cubic centimetres, and the difference between the greatest and smallest 0·6, which gives a range of 6 per cent.

This method of analysis presents the advantages that the amount of material required is very small, and that the time taken to carry out an estimation is short ($1\frac{1}{2}$ hours) compared with the chemical methods.

THE INFLUENCE OF CARCINOMATOUS AND NON-CARCINOMATOUS TISSUES UPON ELECTROSCOPIC LEAK.

By W. S. LAZARUS-BARLOW.

In the following pages are given the results of experiments carried out during the last two years upon the influence of certain carcinomatous and non-carcinomatous tissues upon the electroscopic leak. This inquiry is a necessary part of the entire research as to whether there is any evidence of a connection between radio-activity and the carcinomatous process. The research has been slow because of the small differences that were obtained and the consequent necessity for a large number of observations in order to arrive at conclusions; and further, because the small differences could only be observed in the case of electroscopes the natural leak of which was slow. Where the natural leak was fast, i.e. where the extrinsic causes of discharge were overwhelmingly great, small differences could not be recognized. Hence the observations were carried out on electroscopes of which the natural leak was about 14 mm. on the scale in front of the electroscope in 18 hours, and the actual observations were made for the 6 hours 10.30 a.m.—4.30 p.m. on each of the five days of the week, Monday to Friday. Over the week-end the electroscopes were left entirely at rest, and whenever any new condition was to be examined, whether a new substance or a fresh determination of the natural leak of the experimental electroscopes, the necessary movement of the instrument was carried out on the Friday afternoon, so that a period of two days and three-quarters was allowed for the instrument to come to rest before the fresh set of observations was commenced on the following Monday morning. The control electroscopes were entirely untouched, except for recharging every morning, throughout the entire period of the research. The electroscopes were those used in a research published in the Archives of the Middlesex Hospital, Vol. VII (Fifth Cancer Report), 1906, p. 190, and there described.

The method adopted was to determine the natural leak of the experimental electroscope for a week, then to introduce the substance under investigation and determine the leak for a period of two consecutive weeks, and finally to again determine the natural leak in the absence of the substance. This second determination of the natural leak for a period of one week was followed by a two-week determination of the leak in the presence of some other substance, and so on. Hence the examination of any one substance required in all ten observations of the natural leak, and ten of the leak under the special conditions, and therefore occupied four consecutive weeks. By using the final control week's set of observations as the initial control week's set for the next substance to be examined this period of four weeks was reduced to three in most instances.

In all, ten different electroscopes were used for the research, five of which were charged + and five —. One of each set of five was used solely as a control, and is termed below the "control" electroscope. The remaining four or "experimental" electroscopes were used for examination of the various substances.

The substances examined were liver, kidney, lung, and spleen (four specimens of each) from non-malignant cases, four specimens of hepatic substance from livers the seat of carcinomatous metastasis, four specimens of the inorganic constituents of bones from non-malignant cases, four specimens of the inorganic constituents of bone from cases of carcinoma in one of which the bone itself was the seat of secondary growth, and twelve specimens of carcinoma. Of the carcinomata, four were primary (squamous-cell carcinomata of cervix, tongue and cervix, and spheroidal-cell carcinoma of breast), and eight were metastatic. Of the eight metastatic carcinomata examined six came from the liver, the sites of the primary growth being rectum (three cases each of columnar-cell type), breast (two cases each of spheroidal-cell type), and stomach (one case of spheroidal-cell carcinoma). The remaining two cases were pulmonary metastases from spheroidal-cell carcinomata of breast. The material was derived in four instances from a male, and in eight from females; the ages varied from forty-two years to seventy-five years, and in all cases the diagnosis of carcinoma was open to no doubt, clinical or microscopic. The four cases in which hepatic substance from livers the seat of metastasis was examined were primary spheroidal-cell carcinoma of the breast (two cases), spheroidal-cell carcinoma primary in the liver, and primary squamous-cell carcinoma of the cervix (each one case).

In the majority of cases the material was prepared for examination in the electroscope as follows: Having been freed from adventitious material as far as possible, it was dried in the hot-air oven at 110° C., reduced to a powder, and allowed to stand under acetone for a period of two days; it was then dried in the thermostat at 55° C. until all traces of acetone had disappeared. For the actual electroscopic examination a small quantity of the powder was evenly spread on a disc of lead foil $2\frac{1}{4}$ in. in diameter. In certain cases electrical examination was made of materials that had simply been dried, and subsequently of the residues and the extracts, whether watery, ethereal, or acetone. In the case of extracts evaporation on a water-bath was carried as far as possible before spreading the material on a lead-foil disc.

In a research that has lasted for nearly two years, it cannot be expected that at all times all the electroscopes will have given evidence of the same degree of reliability. In particular, Electroscope XI has shown so marked a lack of correspondence with the others that it is necessary to accept the results obtained from its use with caution. Similarly, Electroscope IX, during a period of nine weeks, at the end of the research showed a remarkable and very regular rise and fall in the leak that was unrepresented in the other electroscopes. With these exceptions the behaviour of the instruments has been very regular.

In order to institute comparisons between the results it was necessary to bring them all to one common standard. This common standard was the arithmetical mean of all the control values of all the electroscopes charged with electricity of the same sign. At the same time the values obtained from day to day in any one electroscope were converted into percentages of the arithmetical mean of the control values of that electroscope. Comparison was then made between the difference between the control and each of the experimental electroscopes (1) in the absence of the substance to be investigated and (2) in its presence.

The degree of reliance to be attached to conclusions derived from consideration of arithmetical means is not the same in all cases. Quite apart from the fact that a large difference between the mean leaks of an electroscope when empty and when containing the substance under investigation is stronger evidence than a small difference, the arithmetical mean may on occasions yield information which is clearly contrary to the greatest amount of evidence afforded by the experiment. This is shown by the following hypothetical case. Suppose that the five observations of leak in the first control week were 11, 11, 11, 11, 11, and again in the final control week were the same, yielding an arithmetical mean for the control period of 11. Suppose, further, that the *experimental* observations made during the two weeks intervening between the two control periods were 20, 10, 10, 10, 10, 20, 10, 10, 10, 10, the arithmetical mean of these values being 12 it would appear that the leak was faster during the experimental period than during the control period, in other words that the substance under investigation accelerated the leak. But inspection of the actual figures shows that this cannot be the case, for on eight of the ten examinations the exact contrary is the truth. To each of these factors due weight has been attached in coming to the conclusions given below, but inasmuch as the results are comparative only and cannot be taken to indicate more than crude differences in behaviour of the substances under investigation, it has been thought advisable to place chief reliance on the arithmetical means, indicating when necessary the degree of support which a consideration of all three factors (arithmetical mean, magnitude of difference from the control, and actual inspection of the values obtained in experiment) affords to information yielded by the arithmetical mean alone.

The Influence of the Same Substance upon the Leak of Different Electroscopes.—In order to determine whether the observed differences in leak of the electroscopes during the control and the experimental periods was due to the substance under investigation, or was accidental, each of the four samples of acetone-extracted spleen used to determine the influence of spleen upon the leak was introduced, on a second occasion, into a different electroscope from that in which the first determination of leak was made. Unfortunately it became clear that the experiment was only partially satisfactory. The values obtained from Electroscope XI must be discarded owing to general unreliability of that instrument, and in particular because one of the gold leaves became detached during the final control period; Electroscope IX was valueless owing to the remarkable rise in leak which it underwent at the time of the second spleen examination; while the entire series of observations constituting the second determination of the leak with spleen (Sept. 21—Oct. 16, 1908) coincided with a heat wave of some intensity. Previous experience had shown that sudden considerable increases of atmospheric temperature are associated with vagaries on the part of the leak of the electroscopes. The information yielded by the experiment is therefore not as conclusive as could be wished; nevertheless, it indicates, in the case of two of the substances at least, that the difference in leak when a substance is introduced within an electroscope is due to that substance, and is not accidental. The arrangement and result of the experiment were as below. "A" signifies that leak was accelerated: "R" that leak was retarded.

Electroscope Number and Charge on Leaves ...		VII. −	XI. +	VIII. −	XII. +	IX. −	XIII. +	X. −	XIV. +
Number of spleen	First series	3	3	4	4	171	171	700	700
	Second "	700	700	171	171	4	4	3	3

RESULTS.

—		Spleen 3.		Spleen 4.		Spleen 171.		Spleen 700.	
		−	+	−	+	−	+	−	+
Influence on leak	First series	R	?	A	A	R	A	A	A
	Second "	R	R	?	R	Same	R	A	?

This experiment shows that Spleens 3 and 700 affect the leaks of the electroscopes in the same way. In the case of Spleens 4 and 171, correspondence is wanting. These must be considered separately. The evidence in favour of acceleration by Spleen 4 in the first experiment is strong, but the evidence in favour of retardation in the second experiment is weak. For the differences between the control and the experimental means in the first series were 8 (electroscope charged —) and 17 (electroscope charged +) in favour of acceleration, and in the actual experiments 7 out of 10 and 8 out of 10 observations respectively showed acceleration, while in the second series with the same substance in another electroscope the difference between the control and the experimental means was only 1, and only 6 actual observations were in favour of retardation, 4 being against it. Similarly in the case of Spleen 171 the evidence in favour of acceleration in the electroscope charged + was great, indeed the difference between the control and experimental means (24) was so great as to rouse suspicion, while the evidence in favour of retardation in the — electroscope of the first series consisted only in the magnitude of the difference between the control and experimental mean values (7), the actual observations being 6 in favour of retardation to 4 against. The evidence in favour of retardation in the + electroscope of the second series was even weaker, the difference between control and experimental means being only 2, and the actual observations being 6 in favour of retardation to 4 against. It is not unreasonable to suppose that the indication for acceleration in the case of Spleen 171 is erroneous, and in that event the correspondence is as good as it is in the case of Spleens 3 and 700, this spleen indicating that it has little or no effect upon the electroscopic leak, and that what effect it has is in the direction of retardation.

Non-malignant Tissues. Spleen.—In view of the consideration that has been given to spleen in the preceding paragraphs, it is not necessary to refer to it here in detail. It is clear, however, that no general statement can be made as to spleen tissue generally, for two specimens showed retardation and two showed acceleration.

Kidney.—Of the four specimens of kidney examined, two led to acceleration of electroscopic leak, whether the leaves were charged + or —; the other two gave discordant results in which the evidence available is so evenly balanced that it is practically valueless.

Lung.—Lung tissue in each of the four cases led to a retardation of electroscopic leak whether the electroscope was charged — or +. The evidence was strong; in the *weakest* case it was supported by a difference of 5 between the control and experimental means, and by 6 actual observations of retardation to 4 of acceleration.

Bone.—Examination of the inorganic constituents of bone shows on the whole that they accelerate the leak of an electroscope, acceleration being shown by five out of seven electroscopes in which four samples were examined. On the other hand two of the samples showed that they did not affect the electroscope in the same way whether it was charged — or +, and in these instances the evidence in favour of a retarding influence was not inconsiderable.

Liver.—The four specimens of liver were examined under different conditions from those under which spleen, kidney, lung, and bone were examined. In the case of bone, the inorganic constituents alone were examined for their influence on leak; while in the cases of spleen, kidney, and lung, organic constituents were examined, but even then only those which were insoluble in acetone. In the case of the liver, the influence upon electroscopic leak was determined of (*a*) the liver itself simply dried and powdered, (*b*) the residue after rigid extraction of the same liver substance with acetone, that is, practically, liver substance less such constituents as are soluble in water or in ether, and (*c*) the acetone extract. It will be convenient to consider these three materials together.

Below are given the results of the experiments, "A" standing for acceleration and "R" for retardation, as before.

Substance.	No. 378.		No. 386.		No. 393.		No. 437.	
	—	+	—	+	—	+	—	+
Liver	A	R	R	R	R	R	R	R
Acetone extract	R	R	R	R	R	R	A	A
Liver residue	R	R	R	R	R	R	R	R

It appears therefore that the liver substance itself and the acetone extract show a strong tendency to cause retardation of the electroscopic leak, and that there is no exception to the rule that the liver residue after extraction with acetone leads to retardation. If the points which have been given above are analysed still further, some additional points of interest appear.

Substance.	No. 378.				No. 386.				No. 393.				No. 437.			
	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.	Difference between control and experimental means.	Observations for and against.
	−	−	+	+	−	−	+	+	−	−	+	+	−	−	+	+
Liver	4 for A	9:1 for A	22 for R	6:4 for R	3 for R	6:4 agst R	17 for R	8:2 for R	5 for R	5:5	25 for R	9:1 for R	7 for R	8:2 for R	23 for R	8:2 for R
Acetone extract ...	5 for R	9:1 for R	8 for R	9:1 for R	6 for R	9:1 for R	10 for R	9:1 for R	7 for R	8:2 for R	11 for R	8:2 for R	4 for A	8:2 for A	1 for A	6:4 agst A
Liver residue	6 for R	10:0 for R	2 for R	10:0 for R	13 for R	10:0 for R	13 for R	10:0 for R	15 for R	8:2 for R	6 for R	10:0 for R	8 for R	9:1 for R	1 for R	9:1 for R

From the foregoing Table it is seen that the evidence for retardation in the case of the liver simply dried and powdered is not so strong as would appear from consideration of the arithmetical means alone. Thus the evidence afforded by the actual observations, as compared with the mean control values of the same electroscopes immediately before and after the experiment itself was carried out, is only slightly in favour of retardation on one out of the eight occasions, is neither for nor against on a second, and is actually against it on a third. After extraction with acetone, however, the case is very different, for it is difficult to imagine a set of experiments which would argue more strongly for the proposition that liver substance after extraction with acetone leads to a retardation of the leak of an electroscope, whether that electroscope be charged

— or +. Concerning the acetone extract itself, it is not necessary here to say more than that it shows a strong tendency to retard electroscopic leak, the evidence for acceleration by means of the acetone extract of Liver 437 being weakened by the contradictory evidence disclosed by analysis of the data for the electroscope charged +. It will be seen later that the acetone extract offers some notable points of resemblance to the watery and ethereal extracts of carcinomatous material in respect of its influence upon the electroscopic leak.

Carcinomatous Material.—The carcinomatous material examined has been dealt with in two ways. Eight of the twelve specimens were extracted with acetone in the same way as the other tissues that have been mentioned already, and the remaining four were examined electrically in stages, viz.: (*a*) in the natural state simply dried and powdered, (*b*) after rigid extraction with ether, and (*c*) after extraction with water subsequent to extraction with ether. This particular experiment was completed by determination of the influence on the leak exerted by the watery extract and the ethereal extract respectively. Since there is probably little difference between the residues after watery followed by ethereal extraction and those after acetone extraction, all twelve extracted samples can be considered together. This will be done after examination of the results obtained in the case of carcinomatous material and extracts made from it.

From the Table on next page it appears that carcinomatous material simply dried and powdered shows a slight tendency to accelerate the leak in certain instances, but that in the main its effect upon the leak is so small, and there is so little correspondence between its action upon electroscopes only differing in respect of the sign of the electrical charge upon the leaves, that it must be concluded that the material, simply dried and powdered, is practically without effect upon electroscopic leak. The effect of extraction of the same substance with ether, and subsequently with water, discloses a remarkable difference. For, whereas the solid residues after extraction afford evidence of an accelerating influence upon the leak which is manifested whether the electroscope be charged — or +, the extracts afford equally strong evidence of a retarding

	No. 31.						No. 67.						No. 75.						No. 106.					
	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.
	–			+	+	+	–	–	–	+	+	+	–	–	–	+	+	+	–		–	+	+	+
Carcinoma, dried and powdered	A	10	8:2 for A	A	6	10:0 for A	R	4	6:4 for R	0	0	6:4 for A	A	11	10:0 for A	0	0	7:3 for A	A	6	7:3 for A	0	0	5:5
Above after extraction with ether	A	—	5:5	A	3	7:3 for A	R	5	8:1 for R	A	6	7:3 for A	A	42	10:0 for A	A	19	10:0 for A	A	11	7:3 for A	A	13	9:1 for A
Above after extraction with Ether and subsequent extraction with water	A	3	9:1 for A	A	7	9:1 for A	A	2	5:5	A	11	7:1 for A	A	19	10:0 for A	A	11	8:2 for A	A	13	9:1 for A	A	7	5:4 for A
Ethereal extract of above	R	10	10:0 for R	R	10	7:3 for R	R	9	9:1 for R	R	16	8:2 for R	R	5	5:5	R	3	7:3 for R	R	9	8:2 for R	R	8	8:2 for R
Watery extract of above after its extraction with ether	R	10	10:0 for R	R	10	5:5	A	2	7:3 agst A	R	7	6:4 for R	A	7	7:3 for A	R	4	8:2 for R	R	8	9:1 for R	R	13	7:3 for R

influence. It is further in support of these conclusions that the evidence for the possession of an accelerating influence by carcinomatous material is greater after it has undergone an extraction by ether and by water than it is when it has undergone extraction by ether alone, and, contrariwise, that the first extract made (i.e. that with ether) has a more pronounced retarding property than that exerted by an extract made subsequently (i.e. the watery extract). It appears therefore that carcinomatous material contains substances which differ fundamentally as regards their influence upon electroscopic leak, and that separation of the two classes of substance can be effected by means of extraction with water and with ether. It will be noted that whereas the extracts from non-malignant liver and carcinomatous material agree in exerting a retarding influence upon electroscopic leak, the residues in the two cases differ fundamentally, the carcinomatous residue exerting an accelerating influence while the hepatic residue exerts a retarding influence.

	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.	Indication of arithmetic means.	Difference between control and experimental means.	Observations for or against.
	–	–	–	+	+	+	–	–	–	+	+	+	–	–	–	+	+	+	–	–	–	+	+	+
Carcinomata (Nos. 31, 67, 75, 106), after extraction with ether and with water.	A	3	9:1 for A	A	7	9:1 for A	A	2	5:5	A	11	7:1 for A	A	19	10:0 for A	A	11	8:2 for A	A	13	9:1 for A	A	7	5:4 for A
Carcinomata (Nos. 473, 501, 548, and 570), after acetone extraction	R	7	8:2 for R	A	2	6:4 for A	A	5	9:1 for A	A	2	6:4 for A	0	0	9:1 for A	A	5	7:3 for A	A	14	7:3 for A	A	3	6:4 for A
Carcinomata (Nos. 99, 174, 240, and 576), after acetone extraction	R	2	5:5	A	11	6:3 for A	R	3	5:5	A	15	8:2 for A	R	5	7:3 for R	A	14	9:1 for A	0	0	7:3 for R	A	11	9:1 for A

From the above Table it appears that six out of the twelve carcinomata examined showed that they possessed the power of accelerating the electroscopic leak whether the charge on the leaves were – or +; that, in addition, one specimen (No. 501) showed that it probably comes into the same class, since the actual observations in the experiments indicate a large preponderance in favour of acceleration, although the arithmetic means for the control period and the experimental period were identical, and of the frankly discordant results three (Nos. 99, 174, and 576) yield evidence in favour of retardation so slight as to be subject to suspicion. Further, the fact that all the electroscopes charged – in the last line of the table show retardation, though in small degree, may easily depend upon a peculiarity of the control electroscope against which each is compared. Examination of the observed values for the control electroscopes during the period in question (April 20—May 15, 1908) shows that whereas the control electroscope charged + gave evidence of a slight rise only (i.e., from a minimum of 35 to a maximum of 40), the control electroscope charged – gave evidence of a rise from a minimum of 45 to a maximum of 59. When working with several electroscopes it is a rule to find that an alteration of atmospheric conditions affects the leaks of all the instruments in the same *direction*, but it frequently happens that the *degree* of rise or fall varies in the different electroscopes, and does not preserve that constant ratio to the natural leak which might be expected theoretically. There is therefore reason to believe that the retardation values indicated for the carcinomatous material in this particular instance are fictitious, and really depend upon the fact that the control electroscope was unduly sensitive to the change and "overshot the mark." If this be so the retardation values for the electroscopes charged – in examination of the carcinomata given in the last row of the table do not tend to negative the conclusion that carcinoma material after extraction with ether and with water, or after extraction with acetone, accelerates the discharge of an electroscope whether the charge on the leaves be – or +.

Hepatic Tissue from Livers the Seat of Carcinomatous Metastasis.—In view of the observations that non-malignant liver tissue after extraction exerts a retarding influence upon the leak, while carcinomatous tissue after extraction leads to acceleration, it became important to determine the influence of the hepatic tissue in livers that were the seat of considerable carcinomatous metastasis. In preparing the material for this investigation great care was taken to exclude carcinoma tissue, and with this object the liver tissue was finely divided and any suspicious portions were discarded. The following results were obtained :—

——	No. 91.		No. 173.		No. 567.		No. 748.	
	−	+	−	+	−	+	−	+
Indications of arithmetic means	R	A	R	R	A	R	R	R
Difference between control and experimental means	4	2	3	4	3	14	3	10
Observations for and against	7 : 3 for R	5 : 5	7 : 3 for R	7 : 3 for R	9 : 1 for A	8 : 2 for R	7 : 3 for R	10 : 0 for R

It thus appears that hepatic tissue from a liver the seat of carcinomatous metastasis tends to retard electroscopic leak; but, apart from the fact that indications of acceleration are recognisable, the evidence in favour of a retarding influence is far less strong than in the case of non-malignant liver. A comparison of the values in the above table with those given for non-malignant liver on p. 125 brings this out clearly.

The Inorganic Constituents of Bone from Cases of Carcinoma.—In one case the bone was the seat of new growth, but in the other three it was unaffected.

——	C. Cervix (bone unaffected).		C. Rectum (bone unaffected).		C. Cervix (bone unaffected).		C. Mamma (bone involved).	
	−	+	−	+	−	+	−	+
Indication of arithmetic means...	A	A	A	A	R	A	A	R
Difference between control and experimental means	4	10	9	9	2	9	7	6
Observations for or against	7 : 3 for A	8 : 2 for A	10 : 0 for A	5 : 5	7 : 3 agst. R	6 : 4 for A	10 : 0 for A	8 : 2 for R

In the case in which the bone itself was affected the results are so discordant that no conclusion is possible. The other three cases afford fairly strong evidence of acceleration, the only example of retardation being doubtful, owing to the smallness of the difference between the control and experimental means, and to the fact that in the actual experiments 7 favoured acceleration and only 3 retardation.

The Electrical Properties of Certain Tissues after Simple Drying and Powdering.—Evidence has been given above that the residue of hepatic or carcinomatous tissue after extraction with acetone, or ether followed by water, exerts a more definite influence on electroscopic leak than the same substance before such extraction. The eight specimens concerning which details are given below were examined electroscopically after simple drying and powdering.

—	Lung, Ref. No. 1, non-malignant.		Lung, Ref. No. 5, non-malignant.		Liver, Ref. No. 2, non-malignant.		Spleen, Ref. No. 3, non-malignant.	
	−	+	−	+	−	+	−	+
Indication of arithmetic means...	R	A	0	A	R	A	A	A
Difference between control and experimental means	2	17	0	5	6	3	7	6
Observations for or against	6 : 4 for R	10 : 0 for A	7 : 3 for A	5 : 5	5 : 5	8 : 2 for A	8 : 2 for A	7 : 3 for A

—	Liver, Ref. No. 8. C. Rectum, no metastases.		Lung, Ref. No. 9. C. Rectum, no metastases.		Spleen, Ref. No. 10. C. Rectum no metastases.		Kidney, Ref. No. 11 C. Rectum, no metastases.	
	−	+	−	+	−	+	−	+
Indication of arithmetic means...	A	A	R	A	A	A	A	A
Difference between control and experimental means	1	8	15	7	5	3	4	2
Observations for or against	5 : 4 agst. A	7 : 3 for A	8 : 2 for R	9 : 1 for A	6 : 2 for A	6 : 4 agst. A	7 : 3 for A	6 : 4 agst. A

It is clear from examination of the above data that the only specimen yielding results of a positive value is spleen from a non-malignant case which exerts an accelerating influence upon the leak. In the remainder there is either frank discordance, or the margin in favour of an influence upon electroscopic leak is so small that it is doubtful whether such differences as were found were not due to experimental error. These specimens therefore agree with the four specimens of liver and four specimens of carcinoma in indicating that the non-extracted substance exerts little or no influence upon electroscopic leak.

CONCLUSIONS.

1. There is strong evidence that carcinomatous tissue which has been extracted with ether and with water, or with acetone, accelerates the leak of an electroscope whether the charge on the leaves be – or +.

2. There is strong evidence that the watery and the ethereal extracts of carcinomatous material retard the leak of an electroscope whether the charge on the leaves be – or +.

3. Carcinomatous material simply dried has little effect upon electroscopic leak. Such evidence as is available indicates that it exerts an accelerating influence.

4. There is strong evidence that non-malignant liver, non-malignant liver after extraction with acetone, and the acetone extract of non-malignant liver, retard electroscopic leak, whether the charge on the leaves be – or +.

5. Hepatic tissue from liver the seat of carcinomatous metastasis after extraction with acetone appears to retard the electroscopic leak to a less extent than hepatic tissue (similarly extracted with acetone) from non-malignant cases.

6. There is strong evidence that pulmonary tissue from non-malignant cases (after extraction with acetone) retards electroscopic leak whether the charge on the leaves be – or +.

7. In the case of splenic and of renal tissue from non-malignant cases (in each instance after extraction with acetone) the evidence is insufficient to allow of any conclusion being drawn.

8. There is evidence that the inorganic constituents of bone from non-malignant cases accelerate electroscopic leak, but the results are somewhat discordant. The inorganic constituents of bone in three cases of malignant disease (the bone not being the seat of metastasis) uniformly accelerated the electroscopic leak whether the charge on the leaves was – or +. In one case in which the bone was the seat of carcinomatous growth the results were inconclusive.

PROTOCOLS OF EXPERIMENTS.

For simplicity all values are expressed as whole numbers, the decimal points being omitted throughout. Thus an actual reading of 5·8 is given as 58.

In the following Tables are given :—

Column A. The observed values uncorrected.

" B. The difference between the observed values of the particular experimental electroscope and the control electroscope, uncorrected.

" C. The indication for acceleration or retardation by the substance in question afforded by the individual observations. This is determined from Column B, the individual differences from the control electroscope being compared with the mean of the two control periods for those observations.

" D. Weekly mean value uncorrected.

" E. Weekly mean expressed as percentage of mean of all control periods of the same electroscope and corrected by the general mean of the control periods of all five electroscopes charged with electricity of the same sign.

Electroscopes VII., VIII., IX. and X., were charged *negatively.*

" XI., XII., XIII., and XIV., were charged *positively.*

The uncorrected means of the control periods of the different electroscopes are as follows :—

Electroscope VII., 62.
" VIII., 50.
" IX., May 14th, 1907, to July 17th, 1908, 42 ; September 21st, 1908, to end, 61.
" X., 51.
" Control charged −, 59.

General mean of control periods of all electroscopes charged −, =53.

Electroscope XI., 62.
" XII., 45.
" XIII., 55.
" XIV., 58.
" Control charged +, 42.

General mean of control periods of all electroscopes charged +, =50.

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Contr Electros		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1907.																							
Control	14 V.	67	+ 1				52	−14				42	−24				55	−11				66		
	15	60	0				52	− 8				40	−20				50	−10				60		
	16	62	+ 3		63	87	50	− 9		51	108	41	−18		41	123	53	− 6		52	106	59	61	
	17	62	+ 4				50	− 9				40	−18				50	− 8				58		
	18	63	+ 2				51	−10				41	−20				52	− 9				61		
Non-malignant tissues simply dried and powdered. Lung in VII. and X. Liver in VIII. Spleen in IX.	21	56	0	R			50	− 6	A			41	−15	A			50	− 6	A			56		
	22	59	0	R			50	− 9	R			43	−16	A			51	− 8	A			59		
	23	60	0	R	60	83	49	−11	R	50	106	41	−19	A	42	126	52	− 8	A	51	104	60	59	90
	24	62	− 1	R			50	−13	R			42	−21	R			50	−13	R			63		
	25	63	+ 6	A			50	− 7	R			41	−16	A			51	− 6	A			57		
	27	63	+ 1	R			51	−11	R			41	−21	R			51	−11	R			62		
	28	57	− 3	R			49	−11	R			41	−19	A			51	− 9	R			60		
	29	59	+ 3	A	60	83	49	− 7	A	50	106	40	−16	A	41	123	50	− 6	A	51	104	56	59	
	30	59	+ 2	A			49	− 8	A			40	−17	A			50	− 7	A			57		
	31	62	+ 2	A			52	− 8	A			44	−16	A			53	− 7	A			60		
Control	3 VI.	61	+ 1				51	− 9				40	−20				51	− 9				60		
	4	61	+ 1				56	− 4				42	−18				52	− 8				60		
	5	64	+ 2		62	85	54	− 8		54	114	42	−20		41	123	54	− 8		52	106	62	60	
	6	63	+ 3				54	− 8				41	−19				52	− 8				60		
	7	62	+ 2				54	− 6				41	−19				52	− 8				60		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1907.																							
Tissues from case of O. rectum without metastases. Liver in VII. Lung in VIII. Spleen in IX. Kidney in X.	10 VI.	62	0	R			50	−12	R			42	−20	R			54	−8	A			62		
	11	64	+2	0			49	−13	R			43	−19	0			51	−11	R			62		
	12	65	+6	A	63	87	51	−8	A	50	106	42	−17	A	43	129	51	−8	A	52	106	59	61	93
	13	63	+1	R			50	−12	R			43	−19	0			52	−10	R			62		
	14	62	+1	R			50	−11	R			43	−18	A			52	−9	A			61		
	17	62	+1	R			52	−9	R			43	−18	A			55	−6	A			61		
	18	62	−1	R			53	−10	R			43	−20	R			53	−10	R			63		
	19	69	+8	A	64	88	49	−12	R	51	108	45	−16	A	44	132	53	−8	A	54	110	61	61	93
	20	66	+4	A			52	−10	R			46	−16	A			54	−8	A			62		
	21	63	+4	A			51	−8	A			45	−14	A			53	−6	A			59		
Control … …	24	65	+3				55	−7				42	−20				55	−7				62		
	25	64	+2				53	−9				46	−16				52	−10				62		
	26	66	+1		66	91	56	−9		55	117	45	−20		45	135	53	−12		53	108	65	64	97
	27	66	+1				55	−10				46	−19				53	−12				65		
	28	68	+2				55	−11				47	−19				54	−12				66		
Carcinoma 31 in VII. " 67 in VIII. " 75 in IX. " 106 in X. Material simply dried and powdered.	1 VII.	61	0	R			52	−9	A			45	−16	A			51	−10	R			61		
	2	61	+1	R			52	−8	A			41	−19	A			53	−7	A			60		
	3	60	0	R	60	83	50	−10	A	51	108	40	−20	A	41	123	51	−9	A	52	106	60	61	93
	4	59	−3	R			51	−11	R			40	−22	R			52	−10	R			62		
	5	60	0	R			52	−8	A			40	−20	A			54	−6	A			60		
	8	62	0	R			49	−13	R			44	−18	A			53	−9	A			62		
	9	65	+7	A			51	−7	A			43	−15	A			55	−3	A			58		
	10	67	+7	A	66	91	49	−11	R	50	106	42	−18	R	42	126	51	−9	A	53	108	60	60	91
	11	69	+8	A			52	−9	A			41	−20	A			54	−7	A			61		
	12	66	+7	A			51	−8	A			40	−19	A			54	−5	A			59		
	15	68	+2	A			52	−14	R			45	−11	A			56	−10	R			66		
	16	68	+2	A			51	−15	R			45	−11	A			53	−13	R			66		
	17	66	+4	A	66	91	48	−14	R	51	108	43	−19	A	44	132	55	−7	A	54	110	62	64	97
	18	68	+7	A			51	−10	A			44	−17	A			51	−10	R			61		
	19	62	−1	R			52	−11	R			44	−19	A			55	−8	A			63		
Control … …	22	61	−8				50	−19				41	−28				54	−15				69		
	23	66	+2				52	−12				41	−23				51	−13				64		
	24	67	+2		66	91	52	−13		53	112	41	−24		42	126	53	−12		53	108	65	64	97
	25	68	+10				53	−5				41	−17				54	−4				58		
	26	68	+2				56	−10				44	−22				55	−11				66		
Control … …	9 IX.	69	+5				57	−7				49	−15				52	−12				64		
	10	66	+3				53	−10				45	−18				52	−11				63		
	11	69	+6		69	95	56	−7		57	121	46	−17		48	144	55	−8		54	110	63	66	100
	12	72	+2				60	−10				51	−19				57	−13				70		
	13	71	+2				58	−11				51	−18				54	−15				69		
Residues of Carcinomata 31, 67, 75, 106, after extraction with ether.	16	72	+5	A			57	−10	R			59	−8	A			60	−17	R			67		
	17	68	+6	A			51	−11	R			54	−8	A			56	−16	R			62		
	18	70	+3	R	70	97	52	−15	R	53	112	53	−14	A	55	165	56	−11	A	57	116	67	65	99
	19	72	+9	A			54	−9	A			56	−7	A			58	−5	A			63		
	20	68	+2	R			53	−13	R			53	−13	A			58	−8	A			66		
	23	69	+5	A			53	−11	R			50	−14	A			56	−8	A			64		
	24	64	+1	R			50	−13	R			52	−11	A			55	−8	A			63		
	25	73	+9	A	70	97	53	−11	R	53	112	56	−8	A	54	162	60	−4	A	58	118	64	66	100
	26	72	+4	R			53	−15	R			59	−9	A			60	−8	A			68		
	27	70	+1	R			55	−14	R			54	−15	A			57	−12	R			69		
Control … …	30	72	0				57	−15				47	−25				56	−16				72		
	1 X.	72	+4				56	−12				47	−21				55	−13				68		
	2	73	+12		72	99	56	−5		56	119	47	−14		47	141	56	−5		56	114	61	66	100
	3	71	+5				55	−11				46	−20				56	−10				66		
	4	70	+5				57	−8				47	−18				56	−9				65		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
Residue of Carcinomata 31, 67, 75, 106, after extraction with ether and subsequent extraction with water.	1907 7 X.	71	+ 9	A			57	− 5	A			48	−14	A			55	− 7	A			62		
	8	70	+ 9	A			51	−10	R			48	−13	A			53	− 8	A			61		
	9	68	+ 8	A	69	95	54	−14	R	54	114	46	−14	A	47	141	55	− 5	A	55	112	60	60	91
	10	69	+11	A			54	− 4	A			46	−12	A			57	−11	R			58		
	11	68	+ 7	A			53	− 8	A			48	−13	A			57	− 4	A			61		
	14	70	+ 2	R			55	−13	R			52	−16	A			59	− 9	A			68		
	15	70	+ 7	A			52	−11	R			47	−16	A			57	− 6	A			63		
	16	69	+ 7	A	69	95	55	− 7	A	53	112	49	−13	A	48	144	57	− 5	A	57	116	62	63	96
	17	67	+ 7	A			51	− 9	A			44	−16	A			56	− 4	A			60		
	18	69	+ 7	A			52	−10	R			46	−16	A			57	− 5	A			62		
Control	21	69	+ 2				55	−12				45	−22				52	−15				67		
	22	71	+ 8				52	−11				45	−18				55	− 8				63		
	23	69	+ 9		69	95	52	− 8		53	112	43	−17		44	132	52	− 8		53	108	60	62	94
	24	68	+ 8				52	− 8				43	−17				52	− 8				60		
	25	69	+ 8				52	− 9				43	−18				54	− 7				61		
Watery extract of Carcinomata 31, 67, 75, 106, after they had been extracted with ether.	28	68	+ 3	R			57	− 8	R			42	−23	R			55	−10	R			65		
	29	66	+ 1	R			56	− 9	R			42	−23	R			53	−12	R			65		
	30	65	+ 1	R	67	92	55	− 9	R	56	119	44	−20	R	45	135	53	−11	R	54	110	64	64	97
	31	67	+ 4	R			56	− 7	A			49	−14	A			55	− 8	R			63		
	1 XI.	67	+ 5	R			55	− 7	A			48	−14	A			54	− 8	R			62		
	4	69	+ 3	R			56	−10	R			50	−16	A			57	− 9	R			66		
	5	70	+ 4	R			57	− 9	R			51	−15	A			57	− 9	R			66		
	6	66	+ 1	R	66	91	56	− 9	R	55	117	49	−16	A	49	147	55	−10	R	55	112	65	63	96
	7	64	+ 5	R			52	− 7	A			45	−14	A			53	− 6	A			59		
	8	63	+ 2	R			53	− 8	R			49	−12	A			54	− 7	R			61		
Control	11	69	+ 8				56	− 5				46	−15				56	− 5				61		
	12	69	+ 9				53	− 7				42	−18				55	− 5				60		
	13	69	+10		69	95	55	− 4		54	114	45	−14		45	135	55	− 4		56	114	59	60	91
	14	75	+14				53	− 8				44	−17				56	− 5				61		
	15	64	+ 4				55	− 5				46	−14				56	− 4				60		
Ethereal extract of Carcinomata 31, 67, 75, 106.	18	66	+ 5	R			53	− 8	R			47	−14	A			55	− 6	R			61		
	19	64	+ 4	R			50	−10	R			45	−15	A			50	−10	R			60		
	20	64	+ 4	R	64	88	53	− 7	R	51	108	46	−14	A	45	135	53	− 7	R	52	106	60	59	90
	21	65	+ 5	R			49	−11	R			44	−16	0			49	−11	R			60		
	22	63	+ 7	R			50	− 6	A			43	−13	A			51	− 5	A			56		
	25	62	+ 3	R			50	− 9	R			41	−18	R			52	− 7	R			59		
	26	61	+ 4	R			47	−10	R			40	−17	R			50	− 7	R			57		
	27	63	+ 5	R	63	87	51	− 7	R	50	106	41	−17	R	41	123	53	− 5	A	52	106	58	59	9[illegible]
	28	62	+ 3	R			51	− 8	R			43	−16	0			51	− 8	R			59		
	29	65	+ 4	R			51	−10	R			41	−20	R			52	− 9	R			61		
Control	2 XII.	66	+ 6				53	− 7				43	−17				53	− 7				60		
	3	68	+ 9				54	− 5				43	−16				55	− 4				59		
	4	65	+ 6		66	91	50	− 9		52	110	43	−16		43	129	53	− 6		53	108	59	59	90
	5	68	+ 9				54	− 5				45	−14				53	− 6				59		
	6	65	+ 6				50	− 9				40	−19				52	− 7				59		
Control ...	1908. 6 I.	58	+ 7				45	− 6				36	−15				45	− 6				51		
	7	58	+ 6				45	− 7				37	−15				50	− 2				52		
	8	57	+ 4		57	79	48	− 5		46	98	36	−17		36	108	46	− 7		45	92	53	51	78
	9	52	+ 4				43	− 5				31	−17				41	− 7				48		
	10	58	+ 4				48	− 6				37	−17				42	−12				54		
Liver from non-malignant case simply dried and powdered.	13	59	+ 9	A			45	− 5	A			36	−14	A			43	− 7	R			50		
	14	60	+ 7	A			47	− 6	A			38	−15	A			43	−10	R			53		
	15	60	+ 7	A	60	83	47	− 6	A	47	100	38	−15	A	38	111	46	− 7	R	46	94	53	53	81
	16	60	+ 6	A			48	− 6	A			37	−17	R			50	− 4	A			54		
	17	61	+ 5	A			49	− 7	R			39	−17	R			46	−10	R			56		
	20	59	+ 5	A			43	−11	R			35	−19	R			45	− 9	R			54		
	21	59	+ 2	R			46	−11	R			37	−20	R			48	− 9	R			57		
	22	55	+ 5	A	58	80	47	− 3	A	46	98	35	−15	A	36	108	45	− 5	A	45	92	50	53	81
	23	60	+ 7	A			47	− 6	A			34	−19	R			44	− 9	R			53		
	24	59	+ 7	A			47	− 5	A			38	−14	A			45	− 7	R			52		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1908.																							
Control	27 I.	59	+ 1				48	−10				46	−18				51	− 7				58		
	28	60	+ 3				50	− 7				39	−18				46	−11				57		
	29	58	+ 3		59	81	48	− 7		49	104	40	−15		40	120	50	− 5		50	102	55	56	85
	30	60	+ 4				51	− 5				41	−15				50	− 6				56		
	31	59	+ 4				50	− 5				39	−16				51	− 4				55		
Acetone extracts of livers investigated Jan. 13 to Jan. 24.	3 II.	57	+ 1	R			48	− 8	R			40	−16	R			51	− 5	A			56		
	4	54	+ 4	A			43	− 7	R			35	−15	A			52	− 2	A			50		
	5	52	0	R	55	76	47	− 5	A	47	100	37	−15	A	38	114	51	− 1	A	50	102	52	54	82
	6	55	+ 1	R			47	− 7	R			38	−16	R			51	− 3	A			54		
	7	56	0	R			50	− 6	R			40	−16	R			50	− 6	R			56		
	10	60	+ 3	R			49	− 8	R			39	−18	R			51	− 6	R			57		
	11	57	+ 1	R			48	− 8	R			39	−17	R			52	− 4	A			56		
	12	57	+ 1	R	57	79	49	− 7	R	49	104	38	−18	R	39	117	51	− 5	A	51	104	56	56	85
	13	55	0	R			49	− 6	R			38	−17	R			51	− 4	A			55		
	14	58	+ 3	R			48	− 7	R			39	−16	R			50	− 5	A			55		
Control	17	58	+ 3				50	− 5				40	−15				51	− 4				55		
	18	60	+ 5				51	− 4				41	−14				51	− 4				55		
	19	58	+ 4		59	81	51	− 3		51	108	40	−14		40	120	51	− 3		50	102	54	55	84
	20	60	+ 5				50	− 5				38	−16				49	− 6				55		
	21	60	+ 5				51	− 4				40	−15				50	− 5				55		
Residues of livers investigated Jan. 13 to Jan. 24 after extraction with acetone.	24	52	+ 1	R			42	−11	R			35	−18	R			45	− 8	R			53		
	25	56	+ 2	R			48	− 6	R			38	−16	R			47	− 7	R			54		
	26	55	+ 2	R	54	75	46	− 7	R	46	98	36	−17	R	36	108	48	− 5	R	46	94	53	53	81
	27	54	+ 1	R			46	− 7	R			37	−16	R			46	− 7	R			53		
	28	54	+ 2	R			47	− 5	R			36	−16	R			46	− 6	R			52		
	2 III.	52	+ 1	R			41	−10	R			34	−17	R			45	− 6	R			51		
	3	50	− 1	R			45	− 6	R			37	−14	A			47	− 4	A			51		
	4	53	+ 3	R	53	73	42	− 8	R	44	93	35	−15	A	35	105	44	− 6	R	46	94	50	51	78
	5	55	+ 3	R			47	− 5	R			36	−16	R			47	− 5	R			52		
	6	53	0	R			44	− 9	R			35	−18	R			47	− 6	R			53		
Control	9	58	+ 2				50	− 6				38	−18				50	− 6				56		
	10	58	+ 6				48	− 4				37	−15				49	− 3				52		
	11	58	+ 2		57	79	49	− 7		48	102	40	−16		38	114	50	− 6		49	100	56	53	81
	12	57	+ 4				45	− 8				37	−16				48	− 5				53		
	13	56	+ 6				47	− 3				36	−14				49	− 1				50		
Carcinomata Ref. Nos. 473, 501, 548, 570, after extraction with acetone.	16	50	− 4	R			45	− 9	R			35	−19	R			50	− 4	R			54		
	17	51	+ 4	R			47	0	A			35	−12	A			47	0	R			47		
	18	52	+ 5	A	51	70	48	+ 1	A	46	98	37	−10	A	36	108	49	+ 2	A	49	100	47	48	73
	19	50	+ 4	R			47	+ 1	A			36	−10	A			50	+ 4	A			46		
	20	51	+ 4	R			44	− 3	A			36	−11	A			50	+ 3	A			47		
	23	56	+ 3	R			50	− 3	A			38	−15	A			50	+ 3	A			53		
	24	54	+ 3	R			49	− 2	A			40	−11	A			51	0	R			51		
	25	56	+ 5	A	54	75	48	− 3	A	49	104	40	−11	A	39	117	51	0	R	51	104	51	52	79
	26	53	+ 1	R			49	− 3	A			37	−15	A			51	− 1	R			52		
	27	53	0	R			51	− 2	A			41	−12	A			51	− 2	R			53		
	30	57	+ 7	A			47	− 3	A			38	−12	A			50	0	R			50		
	31	52	+ 3	R			47	− 2	A			36	−13	A			50	+ 1	A			49		
	1 IV.	52	+ 2	R	54	75	48	− 2	A	48	102	39	−11	A	38	114	48	− 2	R	50	102	50	50	76
	2	57	+ 4	R			50	− 3	A			40	−13	A			52	− 1	R			53		
	3	52	+ 2	R			48	− 2	A			38	−12	A			50	0	R			50		
Control	6	52	0				47	− 5				36	−16				47	− 5				52		
	7	53	+ 7				48	− 2				37	− 9				48	+ 2				46		
	8	54	+ 7		53	73	42	− 5		46	98	37	−10		37	111	45	− 2		47	96	47	48	73
	9	52	+ 5				49	+ 2				37	−10				45	− 2				47		
	10	52	+ 2				46	− 4				37	−13				48	− 2				50		
Control	13	50	+ 3				41	− 6				35	−12				44	− 3				47		
	14	50	+ 5				42	− 3				36	− 9				43	− 2				45		
	15	50	+ 5		50	69	46	+ 1		44	93	37	− 8		36	108	44	− 1		44	90	45	45	68
	16	50	+ 5				45	0				36	− 9				45	0				45		
	17	50	+ 5				45	0				36	− 9				45	0				45		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1908																							
Carcinomata Ref. Nos. 99, 174, 240, 576, after extraction with acetone.	27 IV.	54	+5	A			46	−3	A			38	−11	A			49	0	A			49		
	28	52	+7	A			43	−2	A			38	−7	A			43	−2	A			45		
	29	56	+7	A	56	77	47	−2	A	47	100	38	−11	A	38	114	48	−1	A	49	100	49	50	76
	30	61	+7	A			50	−4	R			37	−16	R			51	−3	A			54		
	1 V.	59	+4	R			49	−6	R			39	−16	R			52	−3	A			55		
	4	60	+1	R			48	−11	R			37	−22	R			51	−8	R			59		
	5	56	+2	R			44	−10	R			37	−17	R			50	−4	R			54		
	6	62	+3	R	59	81	49	−10	R	47	100	39	−20	R	38	114	51	−8	R	50	102	59	56	85
	7	59	+8	A			48	−3	A			37	−14	R			50	−1	A			51		
	8	59	+3	R			44	−12	R			38	−18	R			49	−7	R			56		
Control	11	62	+3				50	−9				39	−20				51	−8				59		
	12	60	+5				48	−7				40	−15				52	−3				55		
	13	60	+4		60	83	46	−10		48	102	38	−18		39	117	51	−5		51	104	56	56	85
	14	57	+3				46	−8				37	−17				49	−5				54		
	15	62	+5				51	−6				40	−17				52	−5				57		
Spleen after extraction with acetone.	18	60	0	R			48	−12	R			40	−20	R			51	−9	R			60		
	19	61	+1	R			48	−12	R			40	−20	R			52	−8	A			60		
	20	59	−1	R	59	81	48	−12	R	48	102	42	−18	R	40	120	51	−9	R	51	104	60	58	88
	21	58	+1	R			48	−9	A			40	−17	0			51	−6	A			57		
	22	58	+5	A			47	−6	A			38	−15	A			51	−2	A			53		
	25	52	−2	R			46	−8	A			39	−15	A			50	−4	A			54		
	26	57	+2	R			47	−8	A			39	−16	A			50	−5	A			55		
	27	60	0	R	57	79	50	−10	A	47	100	43	−17	0	41	123	52	−8	A	51	104	60	56	85
	28	59	+2	R			47	−10	A			41	−16	A			51	−6	A			57		
	29	57	+1	R			47	−9	A			41	−15	A			50	−6	A			56		
Control	1 VI.	68	+4				51	−13				48	−16				54	−10				64		
	2	64	+1				51	−12				46	−17				52	−11				63		
	3	65	−3		65	90	51	−17		51	108	49	−19		48	144	53	−15		53	108	68	65	99
	4	68	−1				52	−17				51	−18				54	−15				69		
	5	61	0				48	−13				48	−13				52	−9				61		
Kidney after extraction with acetone.	8	61	+3	A			50	−8	A			43	−15	A			53	−5	A			58		
	9	62	+2	R			49	−11	A			43	−17	R			51	−9	R			60		
	10	65	+7	A	63	87	48	−10	A	47	100	42	−16	R	42	126	51	−7	A	51	104	58	58	88
	11	64	+3	A			47	−14	R			41	−20	R			50	−11	R			61		
	12	61	+8	A			43	−10	A			41	−12	A			51	−2	A			53		
	15	65	+4	A			48	−13	R			45	−16	R			52	−9	R			61		
	16	67	+6	A			52	−9	A			47	−14	A			55	−6	A			61		
	17	59	+8	A	62	86	48	−13	R	49	104	41	−20	R	44	132	51	−10	R	52	106	61	61	93
	18	59	0	R			47	−12	R			43	−16	R			51	−8	A			59		
	19	62	0	R			49	−13	R			44	−18	R			52	−10	R			62		
Control	22	59	+3				48	−8				42	−14				49	−7				56		
	23	59	−1				49	−11				40	−20				51	−9				60		
	24	62	+5		61	84	48	−9		48	102	42	−15		42	126	52	−5		51	104	57	57	87
	25	60	+4				48	−8				42	−14				51	−5				56		
	26	64	+10				49	−6				44	−10				53	−1				54		
Lung after extraction with acetone.	29	58	0	R			42	−16	R			42	−16	R			51	−7	0			58		
	30	59	−3	R			48	−14	R			43	−19	R			53	−9	R			62		
	1 VII.	62	+3	A	60	83	50	−9	A	48	102	44	−15	A	43	129	53	−6	A	53	108	59	60	91
	2	61	−1	R			52	−10	R			46	−16	R			55	−7	0			62		
	3	60	−1	R			46	−15	R			41	−20	R			51	−10	R			61		
	6	60	−2	R			47	−15	R			43	−19	R			48	−14	R			62		
	7	63	+1	R			48	−14	R			42	−20	R			47	−15	R			62		
	8	60	−3	R	62	86	46	−17	R	47	100	42	−21	R	42	126	50	−13	R	48	98	63	61	93
	9	59	+2	R			47	−10	R			41	−16	R			49	−8	R			57		
	10	66	+6	A			48	−12	R			42	−18	R			48	−12	R			60		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1908																							
Control	13 VII.	64	−2				50	−16				48	−18				54	−12				66		
	14	64	+1				50	−13				43	−20				54	−9				63		
	15	63	+3		63	87	52	−8		51	108	43	−17		45	135	52	−8		53	108	60	62	94
	16	64	+4				53	−7				45	−15				54	−6				60		
	17	62	+2				50	−10				45	−15				52	−8				60		
Control	21 IX.	67	−3				56	−14				59	−11				56	−14				70		
	22	65	−4				52	−17				57	−12				55	−14				69		
	23	63	0		65	90	49	−14		52	110	55	−8		57	81	54	−9		55	112	63	67	102
	24	66	+1				52	−13				57	−8				54	−11				65		
	25	66	0				52	−14				58	−8				54	−12				66		
Spleens investigated May 18–29 re-examined in different electroscopes.	28	63	−1	A			52	−12	A			56	−8	R			52	−12	A			64		
	29	63	0	A			52	−11	A			60	−3	R			52	−11	A			63		
	30	69	−10	R	67	92	55	−24	R	55	117	70	−9	R	70	99	55	−24	R	53	108	79	73	111
	1 X.	68	−10	R			54	−24	R			76	−2	R			54	−24	R			78		
	2	70	−12	R			60	−22	R			87	+5	A			55	−27	R			82		
	5	62	−8	R			57	−13	A			87	+17	A			54	−16	R			70		
	6	61	−5	R			51	−15	R			76	+10	A			50	−16	R			66		
	7	64	−1	A	64	88	56	−9	A	56	119	70	+5	A	76	108	53	−12	A	52	106	65	69	105
	8	67	−1	A			58	−10	A			72	+4	R			54	−14	R			68		
	9	66	−9	R			57	−18	R			76	+1	R			51	−24	R			75		
Control	12	65	−4				54	−15				88	+19				55	−14				69		
	13	65	−4				53	−16				85	+16				55	−14				69		
	14	69	+1		65	90	57	−11		55	117	88	+20		86	122	53	−15		53	108	68	69	105
	15	65	−4				55	−14				87	+18				51	−18				69		
	16	63	−5				55	−13				84	+16				51	−17				68		
Inorganic constituents of bone, Nos. 1, 2, 6, 8. From non-malignant cases in Electroscopes VII., IX., and X.; and from case of C. cervix in Electroscope VIII.	19	62	−10	R			55	−17	R			92	+20	A			56	−16	R			72		
	20	62	0	A			51	−11	A			81	+19	A			49	−13	R			62		
	21	60	+1	A	61	84	49	−10	A	50	106	67	+8	R	72	102	51	−8	A	51	104	59	61	93
	22	60	0	A			47	−13	R			61	+1	R			50	−10	A			60		
	23	59	0	A			49	−10	A			58	−1	R			50	−9	A			59		
	26	60	0	A			50	−10	A			58	−2	R			51	−9	A			60		
	27	61	−1	A			52	−10	A			57	−5	R			53	−9	A			62		
	28	63	0	A	61	84	55	−8	A	52	110	67	+4	R	63	89	53	−10	A	53	108	63	62	94
	29	61	−1	A			52	−10	A			66	+4	R			54	−8	A			62		
	30	59	−4	R			50	−13	R			68	+5	R			54	−9	A			63		
Control	2 XI.	58	−7				53	−12				72	+7				54	−11				65		
	3	62	+3				48	−11				64	+5				51	−8				59		
	4	59	−1		60	83	49	−11		50	106	62	+2		63	89	51	−9		52	106	60	61	93
	5	59	−1				49	−11				61	+1				51	−9				60		
	6	60	+1				48	−11				58	−1				51	−8				59		
Inorganic constituents of bone, Nos. 3, 4, 5, 7. From non-malignant case in Electroscope VII., and carcinomatous in VIII., IX. and X.	9	60	+4	A			48	−8	A			50	−6	R			51	−5	A			56		
	10	60	+5	A			49	−6	A			50	−5	A			50	−5	A			55		
	11	62	+4	A	60	83	50	−8	A	49	104	50	−8	R	51	72	50	−8	A	51	104	58	57	87
	12	59	+1	A			48	−10	A			52	−6	R			50	−8	A			58		
	13	60	0	A			50	−10	A			54	−6	R			53	−7	A			60		
	16	60	+4	A			50	−6	A			58	+2	A			52	−4	A			56		
	17	60	+2	A			50	−8	A			56	2	A			52	−6	A			58		
	18	60	+1	A	60	83	49	−10	A	49	104	56	−3	A	55	78	52	−7	A	52	106	59	57	87
	19	60	+3	A			49	−8	A			51	−6	R			51	−6	A			57		
	20	60	+5	A			48	−7	A			53	−2	A			53	−2	A			55		
Control	23	60	+1				48	−11				52	−7				52	−7				59		
	24	60	0				48	−12				50	−10				52	−8				60		
	25	60	0		60	83	48	−12		48	102	52	−8		51	72	53	−7		52	106	60	59	90
	26	60	+1				47	−12				50	−9				51	−8				59		
	27	60	+1				49	−10				50	−9				52	−7				59		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope VII.					Electroscope VIII.					Electroscope IX.					Electroscope X.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1908																							
	30 XI.	62	−2	R			51	−13	R			58	−6	A			55	−9	R			64		
Hepatic substance after extraction with acetone from livers with C. metastases. Ref. Nos. 91, 173, 567, 748.	1 XII.	60	0	R			48	−12	R			50	−10	A			55	−5	A			60		
	2	60	+1	A	60	83	49	−7	A	49	104	51	−5	A	52	74	51	−5	A	52	106	56	60	91
	3	60	0	R			50	−10	R			50	−10	A			51	−9	R			60		
	4	60	0	R			49	−11	R			49	−11	R			50	−10	R			60		
	7	61	+1	R			48	−12	R			52	−8	A			55	−5	A			60		
	8	60	+2	A			50	−8	A			50	−8	A			50	−8	R			58		
	9	61	+3	A	60	83	48	−10	R	49	104	48	−10	A	50	71	49	−9	R	51	104	58	59	90
	10	60	+1	R			48	−11	R			50	−9	A			51	−8	R			59		
	11	59	+1	R			49	−9	A			48	−10	A			51	−8	R			58		
Control	14	64	+4				51	−9				47	−13				51	−9				60		
	15	60	+2				50	−8				44	−14				50	−8				58		
	16	61	+4		61	84	52	−5		50	106	48	−9		47	67	50	−7		51	104	57	58	88
	17	61	+1				49	−11				46	−14				51	−9				60		
	18	60	+3				50	−7				48	−9				51	−6				57		

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1907																							
Control ...	14 V.	60	12				50	2				60	12				60	12				48		
	15	55	15				47	7				59	19				61	21				40		
	16	58	18		57	74	49	9		49	121	56	16		57	94	62	22		61	91	40	41	116
	17	57	19				49	11				55	17				61	23				38		
	18	57	16				49	8				57	16				61	20				41		
Non-malignant tissues simply dried and powdered. Lung in XI. and XIV. Liver in XII. Spleen in XIII.	21	57	19	A			46	8	A			53	15	R			57	19	R			38		
	22	60	20	A			48	8	A			55	15	R			61	21	A			40		
	23	61	21	A	61	79	49	9	A	49	121	58	18	A	57	94	61	21	A	60	89	40	40	113
	24	63	21	A			52	10	A			60	18	A			60	18	R			42		
	25	65	27	A			51	13	A			61	23	A			60	22	A			38		
	27	65	23	A			49	7	R			61	19	A			61	19	R			42		
	28	62	19	A			49	6	R			59	16	R			58	15	R			43		
	29	59	21	A	61	79	47	9	A	49	121	58	20	A	59	97	57	19	R	59	88	38	40	113
	30	60	23	A			47	10	A			57	20	A			59	22	A			37		
	31	61	22	A			51	12	A			60	21	A			61	22	A			39		
Control ...	3 VI.	60	13				52	5				63	16				63	16				47		
	4	60	17				51	8				62	19				61	18				43		
	5	62	22		61	79	52	12		52	129	63	23		62	102	63	23		62	92	40	43	122
	6	61	18				51	8				62	19				63	20				43		
	7	61	18				52	9				62	19				62	19				43		
Tissues from case of C. rectum without metastases. Liver in XI. Lung in XII. Spleen in XIII. Kidney in XIV.	10	63	23	A			51	11	A			57	17	R			58	18	R			40		
	11	60	21	A			49	10	A			60	21	A			58	19	R			39		
	12	61	19	R	61	79	51	9	A	51	126	60	18	R	59	98	61	19	R	59	89	42	41	116
	13	63	25	A			51	13	A			58	20	A			59	21	A			38		
	14	63	22	A			51	10	A			60	19	R			60	19	R			41		
	17	61	18	R			53	10	A			60	17	R			58	15	R			43		
	18	65	21	A			53	11	A			59	17	R			62	20	A			42		
	19	61	19	R	62	81	50	8	R	52	129	61	19	R	61	101	60	18	R	60	89	42	41	116
	20	62	24	A			52	14	A			61	23	A			60	22	A			38		
	21	62	22	A			51	11	A			62	22	A			60	20	A			40		
Control	24	63	18				52	7				62	17				61	16				45		
	25	61	20				51	10				63	22				62	21				41		
	26	62	21		64	83	50	9		51	126	62	21		62	102	62	21		62	92	41	42	119
	27	67	25				51	9				60	18				61	19				42		
	28	66	25				50	9				61	20				62	21				41		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
Carcinoma 31 in XI. " 67 in XII. " 75 in XIII. " 106 in XIV. Material simply dried and powdered.	1907 1 VII.	62	20	A			50	8	R			62	20	A			60	18	R			42		
	2	61	21	A			49	9	A			61	21	A			61	21	A			40		
	3	60	17	R	61	79	47	4	R	50	123	60	17	R	60	99	60	17	R	60	89	43	41	116
	4	61	19	R			51	9	A			61	19	A			61	19	A			42		
	5	63	23	A			51	11	A			58	18	A			60	20	A			40		
	8	66	23	A			50	7	R			62	19	A			60	17	R			43		
	9	63	22	A			51	10	A			58	17	R			60	19	A			41		
	10	63	20	A	63	82	49	6	R	50	123	60	17	R	60	99	62	19	A	61	91	43	41	116
	11	65	23	A			51	9	A			61	19	A			60	18	R			42		
	12	60	21	A			51	12	A			61	22	A			61	22	A			39		
	15	69	20	A			57	8	R			65	16	R			64	15	R			49		
	16	69	25	A			52	8	R			62	18	A			62	18	R			44		
	17	68	26	A	68	88	52	10	A	53	131	60	18	A	62	102	60	18	R	62	92	42	44	125
	18	67	24	A			52	9	A			61	18	A			61	18	R			43		
	19	67	24	A			52	9	A			62	19	A			62	19	A			43		
Control	22	69	22				53	6				59	12				62	15				47		
	23	60	15				51	6				57	12				60	15				45		
	24	63	21		63	82	51	9		52	128	59	17		60	99	61	19		61	91	42	43	122
	25	60	20				52	12				61	21				62	22				40		
	26	61	19				54	12				62	20				62	20				42		
Control	9 IX.	73	24				53	4				58	9				62	13				49		
	10	63	17				49	3				57	11				59	13				46		
	11	66	13		69	90	51	8		52	128	61	18		61	101	61	18		62	92	43	46	130
	12	70	24				56	10				65	19				66	20				46		
	13	71	23				53	5				62	14				61	13				48		
Residues of Carcinomata 31, 67, 75, 106, after extraction with ether.	16	79	25	A			55	1	R			65	11	R			67	13	R			54		
	17	69	24	A			51	6	A			62	17	A			65	20	A			45		
	18	70	23	A	72	94	50	3	R	52	128	62	15	A	63	104	64	17	A	64	95	47	46	130
	19	70	27	A			52	9	A			65	22	A			63	20	A			43		
	20	70	28	A			51	9	A			63	21	A			62	20	A			42		
	23	66	24	A			51	9	A			66	24	A			63	21	A			42		
	24	61	17	R			48	4	R			66	22	A			66	22	A			44		
	25	68	20	R	68	88	53	5	A	52	128	69	21	A	67	111	69	21	A	66	98	48	46	130
	26	70	22	R			55	7	A			68	20	A			66	18	A			48		
	27	74	27	A			52	5	A			66	19	A			67	20	A			47		
Control	30	79	26				53	0				62	9				64	11				53		
	1 X.	80	30				54	4				62	12				66	16				50		
	2	72	25		73	95	50	3		52	128	59	12		61	101	62	15		63	94	47	48	136
	3	68	23				50	5				59	14				61	16				45		
	4	66	20				51	5				63	17				62	16				46		
Residues of Carcinomata 31, 67, 75, 106, after extraction with ether and subsequent extraction with water.	7	67	17	R			55	5	A			62	12	R			62	12	R			50		
	8	63	14	R			52	3	R			62	13	A			63	14	R			49		
	9	60	13	R	63	82	51	4	0	52	128	58	11	R	61	101	61	14	R	62	92	47	46	130
	10	60	18	R			49	7	A			60	18	A			60	18	A			42		
	11	63	21	0			52	10	A			61	19	A			62	20	A			42		
	14	67	16	R			57	6	A			65	14	A			66	15	R			51		
	15	61	17	R			54	10	A			60	16	A			62	18	A			44		
	16	61	13	R	62	81	52	4	0	53	131	65	17	A	62	102	64	16	0	64	95	48	46	130
	17	60	16	R			52	8	A			60	16	A			62	18	A			44		
	18	59	16	R			51	8	A			61	18	A			65	22	A			43		
Control	21	65	20				51	6				55	10				60	15				45		
	22	62	16				53	7				60	14				62	16				46		
	23	60	14		62	81	50	4		51	126	59	13		59	97	61	15		62	92	46	46	130
	24	61	15				51	5				62	16				65	19				46		
	25	60	11				50	1				60	11				60	11				49		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1907																							
Watery extract of Carcinomata 31, 67, 75, 106, after they had been extracted with ether.	28 X.	62	12	R			52	2	R			62	12	R			62	12	R			50		
	29	62	13	R			55	6	A			62	13	R			63	14	R			49		
	30	63	16	A	63	82	52	5	A	53	131	62	15	A	62	102	64	17	A	62	92	47	48	136
	31	64	18	A			52	6	A			61	15	A			61	15	R			46		
	1 XI.	62	12	R			54	4	R			61	11	R			61	11	R			50		
	4	69	16	A			55	2	R			60	7	R			67	14	R			55		
	5	68	17	A			54	3	R			61	10	R			67	16	A			51		
	6	64	16	A	64	83	53	5	A	53	131	59	11	R	59	97	61	13	R	64	95	48	50	141
	7	59	10	R			50	1	R			57	8	R			60	11	R			49		
	8	59	9	R			51	1	R			59	9	R			67	17	A			50		
Control	11	62	15				53	[illegible]				62	15				62	15				47		
	12	59	12				50	3				59	12				60	13				47		
	13	58	16		59	77	49	7		51	126	59	17		60	99	61	19		61	91	42	46	130
	14	57	8				50	1				60	11				61	12				49		
	15	61	17				51	7				60	16				61	17				44		
Ethereal extract of Carcinomata 31, 67, 75, 106.	18	60	11	A			50	1	R			62	13	R			62	13	R			49		
	19	58	11	A			47	0	R			61	14	R			61	14	R			47		
	20	57	8	R	57	74	47	− 2	R	47	116	59	10	R	61	101	60	11	R	61	91	49	48	136
	21	56	8	R			47	− 1	R			61	13	R			61	13	R			48		
	22	53	4	R			46	− 3	R			60	11	R			61	12	R			49		
	25	52	3	R			45	− 4	R			64	15	R			60	11	R			49		
	26	50	5	R			44	− 1	R			62	17	A			59	14	R			45		
	27	51	9	R	52	68	46	4	A	46	114	62	20	A	62	102	60	18	A	60	89	42	45	127
	28	53	11	A			45	3	A			61	19	A			60	18	A			42		
	29	56	8	R			48	0	R			62	14	R			61	13	R			48		
Control	2 XII.	55	[illegible]				47	1				62	16				59	13				46		
	3	57	14				46	3				63	20				62	19				43		
	4	51	8		53	69	45	2		46	114	61	18		61	101	59	16		60	89	43	45	127
	5	53	[illegible]				46	2				61	17				61	17				44		
	6	60	1				46	− 3				60	11				60	11				49		
	1908																							
Control	6 I.	44	2				40	− 2				50	8				52	10				42		
	7	44	4				40	0				53	13				56	16				40		
	8	45	3		44	57	45	3		41	101	54	12		53	87	56	14		55	82	42	41	116
	9	40	0				41	1				50	10				54	14				40		
	10	44	1				40	− 3				56	13				55	12				43		
Liver from non-malignant cases simply dried and powdered.	13	44	− 2	R			41	− 5	R			50	4	R			54	8	R			46		
	14	46	3	A			42	− 1	R			52	9	R			56	13	R			43		
	15	46	3	A	45	58	42	− 1	R	42	104	53	10	R	52	86	56	13	R	56	83	43	43	122
	16	45	3	A			42	0	A			52	10	R			58	16	A			42		
	17	46	5	A			42	1	A			53	12	A			57	16	A			41		
	20	43	− 3	R			45	− 1	R			55	9	R			56	10	R			46		
	21	41	− 9	R			47	− 6	R			54	1	R			57	4	R			53		
	22	39	− 5	R	41	53	41	− 3	R	44	109	50	6	R	53	87	52	8	R	55	82	44	48	136
	23	41	− 9	R			44	− 6	R			53	3	R			56	6	R			50		
	24	41	− 5	R			42	− 4	R			51	5	R			55	9	R			46		
Control	27	50	6				47	3				58	14				59	15				44		
	28	45	− 3				44	− 4				57	9				59	11				48		
	29	40	0		43	56	41	1		44	109	52	12		55	91	56	16		58	86	40	43	122
	30	41	0				42	1				55	14				57	16				41		
	31	41	− 1				44	3				54	12				58	16				42		
Acetone extracts of livers investigated Jan. 13 to Jan. 24.	3 II.	42	− 3	R			44	− 1	R			56	11	R			58	13	R			45		
	4	39	− 1	R			39	− 1	R			50	10	R			53	13	R			40		
	5	40	− 1	R	41	63	42	1	R	42	104	50	9	R	51	84	54	13	R	57	85	41	43	122
	6	41	0	R			42	1	R			51	10	R			59	18	A			41		
	7	42	− 6	R			42	− 6	R			51	3	R			59	11	R			48		
	10	48	6	A			45	3	A			59	17	A			61	19	A			42		
	11	44	− 1	R			44	− 1	R			57	12	R			60	15	R			45		
	12	42	0	R	43	56	44	2	R	44	109	54	12	R	56	92	59	17	A	61	91	42	43	122
	13	41	− 5	R			42	− 4	R			52	6	R			58	12	R			46		
	14	42	0	R			43	1	R			56	14	A			59	17	A			42		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
Control	1908 17 II.	51	5				47	1				58	12				61	15				46		
	18	45	3				46	4				58	16				60	18				42		
	19	44	2		47	61	46	4		46	114	56	14		58	96	59	17		60	89	42	43	122
	20	47	5				46	4				58	16				60	18				42		
	21	48	6				47	5				58	16				60	18				42		
Residues of livers investigated Jan. 13 to Jan. 24 after extraction with acetone.	24	43	2	R			38	3	R			51	10	R			54	13	R			41		
	25	42	2	R			41	1	R			52	12	R			56	16	R			40		
	26	39	1	R	41	53	40	2	R	40	99	51	13	R	51	84	56	18	A	55	82	38	39	110
	27	41	2	R			40	1	R			51	12	R			55	16	R			39		
	28	41	2	R			40	1	R			52	13	R			56	17	R			39		
	2 III.	39	0	R			39	0	R			50	11	R			55	16	R			39		
	3	40	0	R			41	1	R			52	12	R			54	14	R			40		
	4	40	0	R	40	52	40	0	R	40	99	50	10	R	51	84	55	15	R	55	82	40	40	113
	5	41	1	R			40	0	R			51	11	R			56	16	R			40		
	6	41	2	R			40	1	R			53	14	R			56	17	R			39		
Control	9	49	8				45	4				57	16				59	18				41		
	10	43	4				40	1				53	14				57	18				39		
	11	39	2		42	55	45	8		43	106	54	17		53	87	58	21		57	85	37	39	110
	12	39	2				41	4				51	14				55	18				37		
	13	40	1				45	6				51	12				57	18				39		
Carcinomata, Ref. Nos. 473, 501, 548, 570, after extraction with acetone.	16	45	5	A			41	1	R			53	13	R			53	13	R			40		
	17	39	2	R			38	1	R			50	13	R			51	14	R			37		
	18	37	2	R	39	51	41	6	A	40	99	50	15	A	50	82	51	16	R	51	76	35	36	102
	19	37	2	R			39	4	A			48	13	R			50	15	R			35		
	20	35	0	R			40	5	A			48	13	R			51	16	R			35		
	23	42	4	A			40	2	R			53	15	A			55	17	A			38		
	24	40	3	A			40	3	R			54	17	A			57	20	A			37		
	25	41	1	R	41	53	40	0	R	41	101	54	14	A	54	89	56	16	R	56	83	40	39	110
	26	40	— 2	R			40	— 2	R			53	11	R			55	13	R			42		
	27	41	4	A			43	6	A			54	17	A			58	21	A			37		
	30	45	6	A			43	4	A			55	16	A			56	17	A			39		
	31	41	9	A			41	4	A			52	20	A			54	18	A			32		
	1 IV.	40	5	A	42	55	41	6	A	41	101	51	16	A	53	87	56	21	A	56	83	35	36	102
	2	44	7	A			42	5	A			54	17	A			58	21	A			37		
	3	39	3	A			40	4	A			53	17	A			54	18	A			36		
Control	6	43	6				37	0				52	15				54	17				37		
	7	37	4				39	8				50	17				51	18				33		
	8	40	5		39	51	39	5		38	94	48	14		50	82	51	17		52	77	34	35	99
	9	38	3				37	2				48	13				52	17				35		
	10	39	1				40	2				51	13				52	14				38		
Control	13	41	4				39	2				50	13				51	14				37		
	14	36	0				36	0				48	12				48	12				36		
	15	38	2		37	48	38	2		39	96	49	13		49	81	50	14		50	74	36	36	102
	16	35	0				40	5				49	14				50	15				35		
	17	35	0				40	5				49	14				50	15				35		
Carcinomata, Ref. Nos. 99, 174, 240, 576, after extraction with acetone.	27	42	6	R			40	4	R			53	17	A			57	21	A			36		
	28	41	2	R			41	2	R			53	14	R			54	15	R			39		
	29	41	6	R	44	57	45	10	A	44	109	54	19	A	55	91	57	22	A	57	85	35	37	105
	30	45	7	0			45	7	A			56	18	A			58	20	A			38		
	1 V.	49	12	A			47	10	A			59	22	A			59	22	A			37		
	4	56	16	A			49	9	A			58	18	A			59	19	A			40		
	5	51	14	A			45	8	A			57	20	A			59	22	A			37		
	6	56	17	A	52	68	46	7	A	45	111	59	20	A	58	96	61	22	A	59	88	39	37	105
	7	45	10	A			42	7	A			56	21	A			58	23	A			35		
	8	50	14	A			45	9	A			58	22	A			59	23	A			36		
Control	11	57	17				46	6				55	15				59	19				40		
	12	51	14				44	7				58	21				58	21				37		
	13	49	12		51	66	42	5		44	109	55	20		56	92	58	21		59	88	37	38	108
	14	48	10				41	3				57	19				59	21				38		
	15	50	11				48	9				57	18				61	22				39		

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Control Electroscope.		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
Spleen after extraction with acetone.	1908 18 V.	59	19	R			48	8	A			60	20	A			59	19	A			40		
	19	60	22	R			43	5	R			58	20	A			59	21	A			38		
	20	59	21	R	58	75	48	10	A	46	114	58	20	A	58	96	59	21	A	58	86	38	37	105
	21	58	22	R			46	10	A			56	20	A			58	22	A			36		
	22	51	17	R			43	9	A			56	22	A			57	23	A			34		
	25	60	21	R			44	5	R			58	19	A			56	17	R			39		
	26	58	20	R			46	8	A			57	19	A			58	20	A			38		
	27	61	24	R	60	78	47	10	A	45	111	59	22	A	57	94	58	21	A	57	85	37	37	105
	28	60	23	R			45	8	A			58	21	A			58	21	A			37		
	29	60	24	R			45	9	A			56	20	A			57	21	A			36		
Control	1 VI.	84*	39				50	5				58	13				62	17				45		
	2	95*	53				49	7				57	15				60	18				42		
	3	79*	34		82	107	48	3		48	119	59	14		57	94	59	14		60	89	45	44	125
	4	85*	40				48	3				57	12				60	15				45		
	5	69*	28				47	6				55	14				60	19				41		
Kidney after extraction with acetone.	8	59	17	R			43	1	R			55	13	R			58	16	R			42		
	9	59	20	R			46	7	A			57	18	A			58	19	R			39		
	10	63	24	R	61	79	48	9	A	46	114	59	20	A	57	94	60	21	A	59	88	39	39	110
	11	65	26	A			48	9	A			59	20	A			59	20	A			39		
	12	59	21	R			47	9	A			53	15	R			58	20	A			38		
	15	61	21	R			49	9	A			59	19	A			60	20	A			40		
	16	60	21	R			47	8	A			58	19	A			59	20	A			39		
	17	59	19	R	60	78	46	6	A	47	116	58	18	A	58	96	59	19	R	59	88	40	39	110
	18	60	22	R			45	7	A			55	17	A			58	20	A			38		
	19	60	24	R			46	10	A			58	22	A			59	23	A			36		
Control	22	50	12				43	5				57	19				59	21				38		
	23	51	13				45	7				58	20				60	22				38		
	24	51	13		50	65	43	5		43	106	56	18		57	94	59	21		59	88	38	37	105
	25	49	14				42	7				57	22				59	24				35		
	26	49	13				44	8				58	22				59	23				36		
Lung after extraction with acetone.	29	60	19	A			46	5	R			59	18	R			59	18	R			41		
	30	57	18	A			45	6	R			56	17	R			57	18	R			39		
	1 VII.	52	14	R	54	70	46	8	A	45	111	56	18	R	57	94	56	18	R	58	86	38	40	113
	2	52	12	R			44	4	R			57	17	R			60	20	R			40		
	3	51	10	R			45	4	R			55	14	R			60	19	R			41		
	6	57	14	R			46	3	R			57	14	R			58	15	R			43		
	7	53	15	R			45	7	A			57	19	A			58	20	R			38		
	8	52	13	R	53	69	46	7	A	45	111	58	19	A	57	94	58	19	R	58	86	39	39	110
	9	51	13	R			44	6	R			56	18	R			59	21	A			38		
	10	53	15	R			45	7	A			56	18	R			58	20	R			38		
Control	13	67	21				50	4				59	13				62	16				46		
	14	59	20				46	7				57	18				59	20				39		
	15	57	19		61	79	46	8		47	116	57	19		57	94	59	21		59	88	38	40	113
	16	60	21				47	8				56	17				59	20				39		
	17	60	23				47	10				55	18				55	18				37		
Control	21 IX.						50	0				55	5				58	8				50		
	22						50	3				52	5				60	13				47		
	23						45	6		48	119	54	15		53	87	58	19		59	88	39	43	122
	24						47	8				55	16				60	21				39		
	25						47	7				51	9				59	19				40		
Spleens investigated May 18–29, reexamined in different electroscopes.	28	Observations discarded in this electroscope owing to great variability of leak. Instrument cleaned, new leaves fixed, and observations made in it from November 2nd onwards.					45	9	A			56	20	A			57	21	A			36		
	29						45	4	A			48	7	A			54	13	R			41		
	30						46	— 1	R	46	114	50	3	R	51	84	60	13	R	57	85	47	41	126
	1 X.						45	— 1	R			50	4	0			57	11	R			46		
	2						47	— 3	R			49	— 1	R			56	6	R			50		
	5						46	— 1	R			45	— 2	R			57	10	R			47		
	6						41	1	R			41	1	R			53	13	R			40		
	7						48	[illegible]	A	45	111	49	7	A	45	74	58	16	A	56	83	42	43	122
	8						45	5	A			44	4	0			59	19	A			40		
	9						46	1	R			46	1	R			54	9	R			45		

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* One of the gold-leaves became detached and was readjusted on June 3rd.

TABLE OF EXPERIMENTS—*cont.*

Substance.	Date.	Electroscope XI.					Electroscope XII.					Electroscope XIII.					Electroscope XIV.					Cont Electro		
		A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	D	E
	1908 12 X.						45	— 1				43	— 3				58	12				46		
	13						43	1				40	— 2				50	8				42		
Control	14						42	0		42	104	40	— 2		41	68	55	13		54	80	42	43	122
	15						40	— 3				40	— 3				53	10				43		
	16						42	2				40	0				56	16				44		
Inorganic constituents of Bone, Nos. 1, 2, 6, 8. From non-malignant cases in Electroscopes XI., XIII., and XIV., and from case of C. cervix in Electroscope XII.	19						46	— 4	R			44	— 6	R			55	5	R			50		
	20						42	— 1	R			41	— 2	R			55	12	R			43		
	21						45	3	A	44	109	45	3	R	46	76	52	10	R	55	82	42	43	122
	22						46	6	A			50	10	A			55	15	A			40		
	23						43	4	A			50	11	A			57	18	A			39		
	26						47	2	A			57	8	A			58	13	R			45		
	27						46	7	A			48	9	A			60	21	A			39		
	28						44	4	A	45	111	48	8	A	48	79	58.	18	A	58	86	40	41	11
	29						43	3	A			45	5	A			56	16	A			40		
	30						43	3	A			42	2	R			58	18	A			40		
	2 XI.	138	93				45	0				50	5				59	14				45		
	3	126	86				44	4				50	10				58	18				40		
Control	4	125	85		125	162	43	3		43	106	51	11		50	82	58	18		58	86	40	41	116
	5	123	84				41	2				50	11				57	18				39		
	6	112	72				43	3				50	10				57	17				40		
Inorganic constituents of bone, Nos. 3, 4, 5, 7. From non-malignant case in Electroscope XI., and carcinomatous in XII., XIII., and XIV.	9	85	45	R			44	4	R			57	17	A			58	18	A			40		
	10	84	41	R			45	2	R			57	14	A			57	14	R			43		
	11	94	54	R	97	126	44	4	R	44	109	57	17	A	55	91	55	15	R	54	80	40	40	113
	12	105	67	R			44	6	A			50	12	R			55	17	R			38		
	13	115	75	A			44	4	R			52	12	R			49	9	R			40		
	16	99	63	R			47	11	A			57	21	A			57	19	A			36		
	17	103	62	R			45	4	R			51	10	R			53	12	R			41		
	18	100	60	R	98	127	46	6	A	46	114	56	16	A	54	89	54	14	R	55	82	40	39	110
	19	100	62	R			46	8	A			54	16	A			54	16	R			38		
	20	90	60	R			46	6	A			53	13	R			55	15	R			40		
	23	91	51				46	6				55	15				59	19				40		
	24	88	50				44	8				56	18				57	19				38		
Control	25	94	55		91	118	44	5		45	111	56	17		56	92	56	17		57	85	39	39	110
	26	90	52				45	7				57	19				57	19				38		
	27	92	53				45	6				55	16				57	19				39		
Hepatic substance after extraction with acetone from livers with C. metastases, Ref. Nos. 91, 173, 567, 748.	30	112	67	A			48	3	R			51	6	R			55	10	R			45		
	1 XII.	94	51	A			47	4	R			55	12	R			55	12	R			43		
	2	90	49	A	93	121	47	6	R	47	116	56	15	R	54	89	57	16	R	57	85	41	42	11
	3	88	48	A			48	8	A			56	16	R			58	18	R			40		
	4	80	38	R			47	5	R			54	12	R			58	16	R			42		
	7	88	47	A			47	6	R			57	16	R			58	17	R			41		
	8	83	44	R			46	7	A			55	16	R			57	18	R			39		
	9	81	41	R	83	108	46	6	R	46	114	55	15	R	56	92	56	16	R	57	85	40	40	113
	10	82	43	R			47	8	A			57	18	A			56	17	R			39		
	11	79	40	R			45	6	R			58	19	A			57	18	R			39		
	14	79	38				48	7				57	16				58	17				41		
	15	76	37				47	8				56	17				57	18				39		
Control	16	77	37		77	100	46	6		46	114	58	18		57	94	58	18		58	86	40	40	113
	17	77	39				45	7				58	20				57	19				38		
	18	75	35				46	6				58	18				58	18				40		

ON RETARDATION OF ELECTROSCOPIC LEAK BY MEANS OF RECOGNISED RADIO-ACTIVE AND CERTAIN OTHER SUBSTANCES.

(Supplementary Note.)

By W. S. LAZARUS-BARLOW.

In the "Archives of the Middlesex Hospital," Vol. IX. (Sixth Report from the Cancer Research Laboratories), 1907, p. 78, I described experiments tending to show that uranium nitrate and oxide, thoria, pitchblende, and cholesterin gall-stone affect aluminium plates placed in their proximity for forty-eight hours in such a way that these aluminium plates retard electroscopic leak. The protocols of the experiments are given at the end of the paper.

I have recently examined the observed values in these experiments in respect of the differences from the control values of the experimental electroscopes and the observed values of the control electroscopes in the same way as has been done in the research upon the influence of carcinomatous and non-carcinomatous tissues upon electroscopic leak (this vol., p. 118). The values given in Vol. IX., p. 100, have been expressed as whole numbers and decimal fractions, and the decimal point has been omitted for simplicity. In the following table are given the mean differences during the various parts of the experiments, with the indications of acceleration or retardation afforded by individual observations during the experimental periods when comparison is made with the arithmetic mean value of the control periods of the same electroscope (in brackets).

MEAN DIFFERENCES FROM CONTROL ELECTROSCOPE.

Portion of Experiment.	Uranium Nitrate Electroscope.	Thoria Electroscope.	Cholesterin Gallstone Electroscope.	Pitchblende Electroscope.	Uranium Oxide Electroscope.
Control period I. - -	— 26	— 29	0	— 11	86
„ „ II. - -	— 23	— 31	— 2	— 18	86
„ „ III. -	— 27	— 34	— 6	— 26	86
Mean of all control periods.	**— 25**	**— 31**	**— 3**	**— 18**	**86**
Blank experiment I. -	— 25	— 34	— 4	— 22	86
„ „ II. -	— 25	— 34	— 4	— 21	85
Mean of blank experiment periods.	**— 25**	**— 34**	**— 4**	**— 21·5**	**85·5**
Experiment I. - -	— 28	— 38	— 9	— 25	83
	(8 : 1 for R)	(7 : 4 for R*)	(10 : 1 for R)	(10 : 1 for R)	(5 : 5)
„ II. - -	— 26	— 39	— 7	— 27	81
	(21 : 9 for R)	(30 : 5 for R*)	(31 : 4 for R)	(34 : 1 for R)	(31 : 4 for R)
Mean of experiment periods.	**— 27**	**— 38·5**	**— 8**	**— 26**	**82**

* In the case of thoria the observed acceleration occurred on the first four days of the experiment, and was evidence of the well-known "induced radio-activity" due to thorium.

This method of considering the values obtained by experiment therefore confirms the conclusion arrived at elsewhere (loc. cit., p. 87) that aluminium discs which have been placed in proximity to uranium oxide, uranium nitrate, thoria, pitchblende, and cholesterin gallstone have acquired the property of retarding electroscopic leak as the result of their exposure to the substances named.

THE INFLUENCE OF RADIO-ACTIVITY ON THE DIVISION OF ANIMAL CELLS.

BY W. S. LAZARUS-BARLOW AND VICTOR BONNEY.

IN the research described below an attempt has been made to determine whether radio-activity influences the rate of division of animal cells. Experiments have already been made on this subject, notably in connection with X-rays, and of these the most satisfactory results are those published by Perthes.* This author, after pointing out that previous workers had obtained discordant results, some asserting that the rays accelerate, others that they retard the rate of division, carried out a series of experiments using a more or less known "dose" of the rays. Thus he exposed the cells to an amount corresponding to one-fifth of the amount that normal skin will take without dermatitis, i.e. one-fifth of a Sabouraud pastille dose, and found that the ova of *Ascaris megalocephala* (parasitic in the horse) are inhibited in their development. This inhibition, according to Perthes, may be complete, so that the ovum never develops at all, but more commonly, is relative, in that the early stages of development take place in the ordinary fashion, but pass insensibly into a disorderly development which shows itself in the formation of a large number of monstrosities devoid of movement, instead of the formation, as in the control, of well-formed active embryos within the egg-case. It will be seen that we fully confirm Perthes's observations, but are convinced that he is wrong in denying the occurrence of acceleration.

Cattley, in a paper read before the Leeds meeting of the Pathological Society of Great Britain and Ireland (January 1909) and to be published in the "Journal of Pathology and Bacteriology," reported the results of experiments he had made upon the action of X-rays upon the cells of the growing root-tip of certain plants. He found that the X-rays have a stimulating action on the growth of the tissues, the maximum of which is reached after a single exposure of about 30 minutes' duration. With exposures of longer duration the stimulant action is less marked, and after an exposure lasting two hours the rate of cell-division is less than in the controls. Studying the cytological changes he found that they consist chiefly in an increase of the number of cells undergoing mitotic division, with a tendency to precocious splitting of the spiremes and subsequent modifications in the characters of the metaphase and anaphase. In all cases, however, the rate of growth resumes its normal proportions a few hours after the termination of single or multiple exposures to X-rays, and no ultimate gross pathological changes are produced by repeated long exposures. Having regard to the differences in the type of cell employed, and to probable differences in the degree of exposure of the cells to radio-active action in Cattley's experiments and our own, the agreement in our conclusions is significant. The only important point of difference is the absence of gross pathological change in the case of vegetable cells, and its extensive presence in the case of animal cells, as the result of exposure to the rays.

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* "Wien. klin. Wochenschr." 1903, pp. 668 and 715.

The experiments have been carried out on the ova of Ascaris, in some cases at a temperature of 37° C., in others at that of the room; and in the latter instance certain of the experiments were carried out in summer, others in winter. By this means it was possible to allow the changes to progress with sufficient slowness for satisfactory examination, and also to allow of the action of a radio-active material (e.g. radium) for a longer time. Experiments were carried out in connection chiefly with X-rays, but also with radium, thorium, and uranium.

In the earliest experiments the ova were suspended in a small amount of saline solution for exposure to the rays and for examination; later it was found that development takes place well if the fluid medium be 1% boracic acid, and inasmuch as it was necessary to examine the same cells on successive occasions the following procedure was adopted: Ova obtained from the two oviducts close to their junction were spread on the surface of coverslips or of small Petri dishes the lower portions of which were plane and polished, a small amount of water being added in order to obtain a layer of ova one cell thick. This was allowed to dry, and after or before exposure to the radio-activity, according to circumstances, was covered with a layer of 10% gelatine made up with 1% boracic acid instead of water and allowed to set. In such a preparation the ova can be easily examined with an inch objective, while the small amount of antiseptic prevents the growth of moulds almost entirely, and allows an experiment to extend over ten or twelve days. With experiments of this duration it is advisable to invert the Petri dish over moistened filter paper while not actually under observation.

In the case of exposure to X-rays the ova were spread out on a number of coverslips and allowed to dry. One of these was taken for a control, and the remainder were arranged in a circle beneath the Crookes tube in such a way that all were as nearly as possible equidistant from the anticathode. The apparatus was then started, and at 2 min., 4 min., 6 min., 9 min., 12 min., 15 min., and 20 min., was momentarily stopped in order that one of the coverslips might be removed. In this way it was possible to obtain an increasing intensity of action, since it was certain that each coverslip had been exposed to the same amount of rays as its predecessor and something more. Owing to the variations in the amount of rays emitted by the same tube from time to time this method was thought better than uninterrupted exposures of individual coverslips for definite periods. In the case of radium, thorium, and uranium, the ova were exposed to the powdered substance without any intervening substance other than the gelatine during the entire length of the experiment.

Exposure to X-rays.

Below are given the values obtained in a typical experiment in which the ova were exposed to X-rays. It must be noted that different values were obtained in different experiments, probably owing to differences in the amounts of rays given off by the tube, and possibly owing to differences in the degree of maturation of the ova at the time when they were obtained for experiment.

CHARACTERS OF CELL-DIVISION IN 200 OVA AFTER EXPOSURE TO X-RAYS FOR VARYING PERIODS.

Immediately after exposure.

All cells in 1-cell stage.

Twenty-four hours after exposure (room temperature, 23 September 1908).

	1-cell stage.	2-cell stage.
Control	157	43
2 min. exposure	140	60
4 ,, ,,	151	49
6 ,, ,,	164	36
9 ,, ,,	175	25
12 ,, ,,	184	16
15 ,, ,,	187	13
20 ,, ,,	194	6

Forty-eight hours after exposure (room temperature, 24 September 1908).

	1-cell stage.	2-cell stage.	3-cell stage.	4-cell stage.
Control	74	65	26	35
2 min. exposure	71	52	22	55
4 ,, ,,	81	42	21	56
6 ,, ,,	90	46	20	44
9 ,, ,,	107	53	21	19
12 ,, ,,	102	60	17	21
15 ,, ,,	128	43	14	15
20 ,, ,,	116	57	13	14

This experiment, which has been repeated on many occasions, shows conclusively that the X-rays have a dual effect. Short exposures accelerate, long exposures retard cell division.

Inasmuch as the ovum does not increase in size during the processes of cell-division, it becomes difficult to determine the number of cells present after the 4-cell stage has been reached, confusion between a morula and a 1-cell stage being somewhat difficult to avoid. With the formation of an embryo, however, differentiation between the control and the exposed cells becomes possible. Thus in another experiment, which passed through a course practically identical with that given in detail above in its early stages, the later stages were as follows:—

Third and fourth days after exposure to X-rays, the ova kept in the incubator at 37° *C.*

Control	showed immature	embryos	and	1	moving	worm in egg case.
2 min.	,,	,,	,,	1	,,	,,
4 ,,	,,	,,	,,	1	,,	,,
6 ,,	,,	,,	,,	3	,,	,,
9 ,,	,,	,,	,,	6	,,	,,
12 ,,	,,	,,	,,	1	,,	,,
15 ,,	,,	,,	,,	2	,,	,,
20 ,,	,,	,,	,,	21	,,	,,

After keeping the ova for a further period of three days in the incubator at 37° C. the condition was as follows:—

Control	showed complete development of	193	ova and failure of development in	7 ova.
2 min.	,,	193	,,	7 ,,
4 ,,	,,	169	,,	31 ,,
6 ,,	,,	166	,,	34 ,,
9 ,,	,,	165	,,	35 ,,
12 ,,	,,	174	,,	26 ,,
15 ,,	,,	157	,,	43 ,,
20 ,,	,,	133	,,	67 ,,

Further, in order to determine the actual condition of the embryos as to life, examination was made of the control and the 20-minute specimens on the warm stage, and actual movement of the embryo within the egg case was watched for. Absence of life was only concluded when a continuous observation of a cell for 20 minutes on the warm stage failed to reveal movement, a length of time that was probably sufficient, since the movements of undoubtedly living embryos on the warm stage are very active. The result was as follows:—

Control—Of 50 complete embryos, 45 showed movement, 5 showed no movement.

20 min.—Of 50 complete embryos, 30 showed movement, 20 showed no movement.

It follows from these experiments that although X-rays inhibit the cell-division and ultimately lead to the formation of a smaller number of living embryos than in the control specimen, yet the first appearance of actual moving embryos takes place in ova that have been exposed to X-rays. As will be seen later, the same phenomenon occurs when the ova are exposed to the action of radium.*

Exposure to Uncovered Radium.

The experiment given below lasted for 15 days, during the last 4 of which the ova were in the incubator at 37° C., while during the first 11 they were exposed to the room temperature in December. The ova exposed to radium were placed under conditions as far as possible identical with those to which the control ova were exposed, and the action of the radium on the latter was prevented by protecting them with a thick sheet of lead. The final incubation of the ova was to ensure that all the ova which were on the way to develop into worms or had still the capability of development should do so. It was desired to determine the changes taking place in a single series of cells, and with this object the same field of ova was photographed on successive days. During the first 10 days this was successfully done, but after that time changes occurred in the gelatine as the result of a temperature at 37° C., which rendered photography impossible in that field. Consequently other fields were chosen for photographic record. It is believed that no essential error has been thereby introduced, except that the number of living worms found in the specimen exposed to radium is somewhat too low. In addition to obtaining results from the photographic records (and these are the source of the figures given below) counts of not fewer than 200 ova were made daily; these will not be reproduced here, since they agree substantially with the values derived from the microphotographs. The only important difference is that the radium-exposed ova yielded 4% of living worms, and not 1% as indicated by the final microphotograph. (See Plate.)

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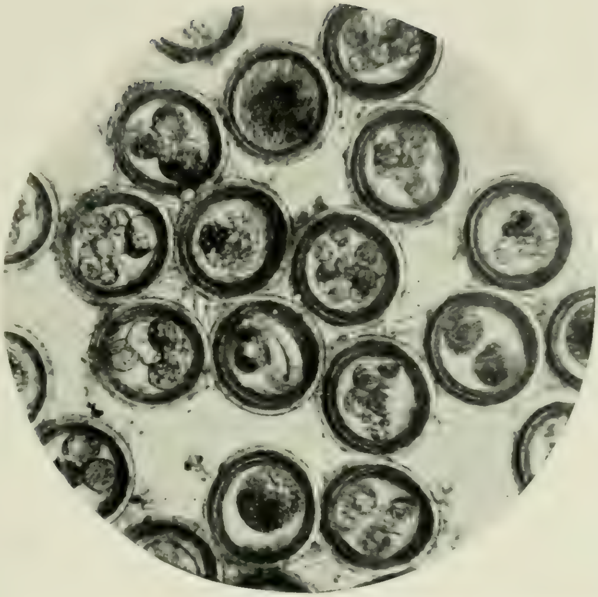
* A few attempts were made to determine whether the formation of monstrosities is associated with irregular mitotic division of the cells, as seems probable; but the fact that the division is not accompanied by growth of the daughter-cells rendered satisfactory observations impossible.



DEVELOPMENT OF OVA OF ASCARIS MEGALOCEPHALA UNDER THE INFLUENCE OF RADIUM.

Note the fully-developed embryo in the centre and the great irregularity of division in the remaining ova.

CHARACTERS OF CELL-DIVISION IN OVA EXPOSED TO THE ACTION OF RADIUM.

Day and Hour.	Control ova. Percentages.								Ova exposed to Radium. Percentages.								Remarks.
	Number of cells in field.	1-cell stage.	2-cell stage.	3-cell stage.	4-cell stage.	Morula stage.	Incomplete embryos.	Living worms.	Number of cells in field.	1-cell stage.	2-cell stage.	3-cell stage.	4-cell stage.	Morula stage.	Incomplete embryos.	Living worms.	
0, 12 noon	92	100	—	—	—	—	—	—	60	100	—	—	—	—	—	—	
1, 12 noon	92	99	1	—	—	—	—	—	60	88	12	—	2	—	—	—	
3 p.m.	69	94	6	—	—	—	—	—	79	90	6	—	4	—	—	—	
5 p.m.	67	84	10	1	5	—	—	—	81	93	4	—	3	—	—	—	Position chosen for successive observations
2, 10 a.m.	65	72	12	1	12	—	—	—	81	81	14	1	4	—	—	—	
4, 10 a.m.	71	56	20	1	7	16	—	—	81	61	24	1	10	4	—	—	
5, 10 a.m.	67	58	9	—	12	21	—	—	81	61	19	4	11	5	—	—	
7, 10 a.m.	62	55	5	3	10	27	—	—	84	56	12	9	14	11	—	—	
11, 10 a.m.	63	44	8	6	15	21	6	—	82	46	6	5	22	16	1	4	
15, 10 a.m. after 4 days 37°	101	61	5	1	5	10	—	18	65	63	1	6	3	26	—	1	Different fields from above.

From this experiment it is clear that the results of exposing ova to the action of radium are identical in character with those obtained on exposure of the ova to X-rays. That is to say, the action of radium is to accelerate the division of the cells in an early stage so that the 4-cell stage appears earlier than in the control, while the actual appearance of living worms also occurs earlier in the case of ova exposed to radium than in the control. On the other hand, the radium also exerts a pronounced inhibitory action, as shown by the fact that a considerably smaller number of ova develop into fully-formed living worms if the ova have been exposed for a long time to radium than if they have not been so exposed. Irregular divisions of the cells and the formation of monstrosities which have already been described by Perthes in the case of exposure to X-rays, both of which we fully confirm, are also found in the case of ova exposed to radium.

Exposure to Thorium and Uranium.

The results of exposing ova to the action of the emanation and radiations of thoria or to the radiations of uranium are not nearly so marked as those which follow exposure to X-rays or radium. This might be expected, considering the far smaller radio-active power of the former substances. Indeed, the effects are mainly comparable with those produced by small exposures to X-rays or radium, and consist chiefly in slight but definite acceleration. Nevertheless, evidence of an inhibiting action is not wanting, though it does not lead to a complete arrest of development on the part of the ova for as many ova exposed to the action of thoria or uranium finally develop into living worms as occurs in the control, but arrive at that complete development later than the control ova.

The following experiment illustrates these points:—

29 *September* 1908.—Ova exposed to the action of thoria and uranium oxide. Exposure continued throughout entire experiment. All ova in single-cell stage.

30 *September* 1908.

Control .	. showed	157	one-cell	and	43	two-cell stages in 200 ova.
Thorium-exposed	,,	136	,,	,,	64	,,
Uranium-exposed	,,	141	,,	,,	59	,,

1 *October* 1908.

Control .	. showed	0	one-cell,	17	two-cell,	183	four - cell (and over) stages.
Thorium-exposed	,,	4	,,	21	,,	175	,,
Uranium-exposed	,,	3	,,	10	,,	187	..

2 *October* 1908.

Control . .	All cells in morula stage.
Thorium-exposed Uranium-exposed	All cells in morula stage, but the morula appears to be composed of fewer cells than in the control.

8 *October* 1908.

Control .	showed	115	complete living	and	85	incomplete embryos.
Thorium-exposed	,,	42	,,	,,	158	,,
Uranium-exposed	,,	81	,	,,	119	,,

11 *October* 1908.—The thorium-exposed and the uranium-exposed ova were indistinguishable from the control, since all three specimens consisted of fully-developed living worms.

CONCLUSION.

As a result of the facts indicated above, we conclude that the action of X-rays, radium, thorium, and uranium, upon the animal cell as exemplified by the ova of *Ascaris megalocephala* of the horse is two-fold. In small doses or continued for a short time it causes division to proceed at a faster rate than normal; in larger doses evidence of an inhibitory power is given which may lead to total arrest of development at some varying period after the cycle of changes leading to the formation of the embryo has commenced. At the same time the formation of monstrosities and of irregular divisions indicates that the cell exposed to the action of the radio-active substance enters on a disorderly cycle of changes. It is possible that the antagonistic effects of favouring and of inhibiting cell-division may be extremes of one single property of the radio-active substance, but the fact that both influences are seen at work at the same time may indicate that the radio-active substances possess two distinct properties which are capable of acting on the ova independently.

THE INFLUENCE OF ATOMIC WEIGHT AND VALENCY UPON THE RADIO-ACTIVITY OF URANIUM AND THORIUM COMPOUNDS.

By W. S. LAZARUS-BARLOW and H. A. COLWELL.

In the course of an investigation into the nature of the substance present in certain animal tissues, which affects a photographic plate in the dark, it was considered possible that the property might be strictly radio-active, but modified owing to the combination of the radio-active material with a protein substance. It was therefore decided to prepare albuminous compounds of a recognised radio-active substance and examine such compounds electrically and photographically. As a result of preliminary experiments it was seen that the subject required a more extensive examination, and that it was necessary to prepare a number of inorganic uranium compounds (uranates) in order to obtain a sufficiently comprehensive series. Ultimately the research was carried out upon the sulphates and nitrate of uranium and the uranates of lithium, ammonium, sodium, potassium, thallium, calcium, strontium and barium, as inorganic uranium compounds, and upon the precipitate formed on mixing uranium nitrate in solution with egg-white, Witte's peptone solution, and serum from a pleural effusion, as organic uranium compounds. Experiments were also made with the sulphate and nitrate of thorium and with a thorium-egg-white compound.

Method of Preparing Compounds.—For the preparation of the inorganic uranates the alkalis and the alkaline earths were chosen because they all form soluble hydroxides, which, on the addition of a soluble salt of uranium, produce a precipitate that, after standing for a time, possesses the general formula $U_2O_7X_2$ or U_2O_7X according as X is a monovalent or a divalent element. It is necessary in the preparation of these uranates that the supernatant fluid shall be slightly but definitely alkaline throughout the process, and in the actual experiments it was considered that the admixture of a minute amount of uncombined alkali with the uranate was less important than the possibility of hydrolysis if the precipitate were washed with water. For this reason the only washing of the precipitate that took place was with the dilute alkaline hydroxide used for making the uranate. The precipitate was collected on a filter paper, dried at 55° C., reduced to a fine powder, and kept in a corked bottle. The alkaline and alkali earthy hydroxides were freshly prepared, and the purest material obtainable was used. The same samples of uranium nitrate and of thorium nitrate were used throughout the research for preparing the various compounds.

The albuminous compounds of uranium and of thorium were made by allowing a solution of the nitrate to fall, drop by drop, into the albuminous fluid with constant stirring, and the addition of the nitrate was stopped while some of the albuminous fluid was still uncombined. A copious curdy precipitate was obtained in this way, which was subsequently dealt with either by direct drying at 55° C. or by drying at 55° C. after standing under acetone for two hours. Ultimately the last-mentioned method was regularly adopted, since it facilitates drying and powdering, and also removes any uncombined uranium or thorium nitrate. The amount of uranium in the albuminous compound was subsequently determined volumetrically, and the amount of thorium gravimetrically after incineration.

In the case of certain of the experiments in which it was desired to make comparison between certain inorganic salts of either uranium or thorium a special course was necessary. In comparing the rates of electroscopic leak in the presence of uranium sulphate and nitrate, for example, it was not sufficient to prepare a sulphate from the nitrate and compare that with the original nitrate; it was necessary to prepare an oxide from the nitrate, and from this common stock to prepare not only the sulphate but also a fresh nitrate. It is only this freshly prepared nitrate which is in reality derived from the same stock of uranium as the sulphate. The adoption of this routine is, if possible, more important in the case of thorium compounds owing to the presence of thorium X in the filtrate and its absence from the thorium hydroxide formed on the addition of ammonia to a solution of a thorium salt (Rutherford and Soddy).

The Electrical Methods.—The electrical effects of the various compounds were determined by testing the leak of an earthed, lead, gold-leaf electroscope of the kind used by one of us in other researches and fully described in Vol. VII. of the Archives of the Middlesex Hospital (Fifth Cancer Report), 1906, p. 190. The powder was placed in a shallow aluminium (or, for certain experiments, platinum) dish about 18 mm. square and ·75 mm. deep, and the situation of the dish beneath the electroscope was fixed by metal stops. The powders were composed of particles of fairly uniform size, since all passed through a fine-meshed platinum gauze before being used. The leak was over a constant distance of 10 mm. on the scale in front of the aperture of the electroscope, and the times were taken with a stop watch. For the purposes of the research over 700 observations of leak were made in all.

The Electrical Results.—The electrical experiments were carried out on two varieties of material: (1) substances prepared in the way mentioned above, and (2) the same materials after they had been raised to a white heat for a considerable time on a platinum dish. In the case of the uranates, with the exception of the ammonium salt, the results of electrical examination of the unheated and heated substances are very similar, but in the case of all the other uranium compounds, including ammonium uranate, and all the thorium compounds a marked difference obtains whether the substance is examined in the natural state or after incineration. That is to say, a great difference shows itself according as the substances under examination are thermostable or thermolabile.

In making a number of electroscopic investigations on successive days and over a long period the actual readings obtained for a given substance are found to vary somewhat. Nevertheless the relative rates of discharge of the electroscope in the presence of the various substances are extraordinarily constant. Hence, though on a given day the actual readings obtained for the series of uranates, for example, may differ a little on one side or other of the mean values, yet the sequence of the rates will always be the same. To this statement, which we have confirmed on many occasions, we have only found one exception, namely, that of lithium uranate. Although one sample of lithium uranate took its proper place in the series for the first few days after its preparation, it failed to do so subsequently, and instead of leading to a more rapid leak than sodium uranate, it, and all other samples of lithium uranate we prepared from the same stock of lithium, yielded a slower leak than sodium uranate. This anomaly did not affect the mean values, and only showed itself in the case of the unheated material; it was probably, therefore, accidental.

In Table I. are given the means of the entire series of observations upon the unheated and strongly heated materials, with the mean rate of leak per hour of the electroscope in the presence of the substance in question.

TABLE I.

Mean Values of Electroscopic Leak in the presence of various Uranium and Thorium Compounds in the Natural State and after Strong Heating.

Substance in Electroscope.	Mean Time required to Leak 10 mm.				Mean Rate of Leak per hour in mm.	
	Natural State.		Incinerated.		Natural State.	Incinerated.
	min.	sec.	min.	sec.		
Uranium oxide (black), U_2O_5 … …	3	25	3	23	175	177
Lithium uranate, $U_2O_7Li_2$ … …	4	11	3	48	143	158
Ammonium uranate, $U_2O_7(NH_4)_2$ …	4	48	3	30	125	171
Sodium uranate, $U_2O_7Na_2$ … …	4	15	3	54	141	154
Potassium uranate, $U_2O_7K_2$ … …	4	23	4	33	137	132
Calcium uranate, U_2O_7Ca … …	4	46	4	37	126	130
Strontium uranate, U_2O_7Sr … …	5	6	4	58	117	121
Barium uranate, U_2O_7Ba … …	4	56	4	42	121	128
Thallium uranate, $U_2O_7Tl_2$ … …	5	57	5	16	101	114
Uranyl sulphate, $UO_2(SO_4)$ … …	6	36	3	23	91	177
„ nitrate, $UO_2(NO_3)_2$ … …	7	30	3	13	80	187
Uranous sulphate, $U(SO_4)_2$ … …	9	41	3	48	62	159
Uranium—Witte's peptone … …	26	47	4	47	22·4	126
„ serum (pleural fluid) …	44	27	7	2	13·5	85
„ egg-white … … …	46	9	6	19	13·0	95
„ „ (digested) …	47	34	22	39	12·6	26·5
„ spleen pulp … … …	55	3	11	23	10·9	53·6
Thorium sulphate, $Th(SO_4)_2$ … …	9	13	4	37	62	124
„ nitrate, $Th(NO_3)_4$ … …	11	0	4	14	55	142
„ egg-white … … …	80	0	14	29	7·5	41·4

Natural leak of empty electroscope 3·6 per hour.

The most striking differences between the values obtained for the unheated and the strongly heated materials concern the sulphates and nitrates and the entire series of albuminous compounds. These latter are yellow dull powders as obtained in the dry state, but when they are heated in a platinum basin they char in the ordinary way, and after the carbon has been completely burnt off a bright yellow, greyish, or black powder entirely soluble in dilute nitric acid (presumably oxides of uranium) is left. Heating of the inorganic uranates, excluding the ammonium compound, does not lead to the same changes, and in particular there is no obvious diminution of volume as in the case of the albuminous compounds. The materials, however, change colour with strong heating. Whereas the freshly prepared, dried, and powdered salts are all of a bright canary yellow or slightly orange tint, on strong heating the lithium salt becomes olive-green, the sodium a deep orange-chocolate, the potassium a bright orange, the calcium a deep olive-green, the strontium a yellowish sage-green, the barium an olive-green, and the thallium a bright orange red, almost a vermilion. These colours persist without change, and the powders are not hygroscopic. The latter point was somewhat unexpected owing to the presence of a small excess of the alkaline hydroxide used in the preparation of the uranates, and it is still possible that some part of the differences in rates and the occasional discrepancies between the rates of the lithium and the sodium salts may depend upon small and variable differences in this direction. In any case there is a probability that the distinct colour differences between the different uranates indicate that they are stable compounds which can undergo strong heating unchanged or almost unchanged. For if they were disintegrated by the heat the result should probably be a mixture of uranium oxide (yellow or black), with an oxide of the alkali or alkaline earth (white). With the albuminous compounds the case is quite different, for it is certain that a complete disintegration occurs with a disappearance of the entire protein molecule, such small admixture of salts as are present in the egg-white, etc., being negligible, and the resulting ash containing all the uranium.

The effects of incineration will be considered later, attention being now confined to the uranates.

Uranates of the Alkalis and Alkaline Earths.—The figures given in Table I. necessitate a reconsideration of the view generally held that the relative radio-activities of a variety of compounds of uranium depend upon the percentages of uranium present in those compounds. Such a statement is only partially true, for it is clear that the percentage of uranium in a compound is not only dependent upon the amount of uranium, but also upon the other constituents of the molecule. It was for this reason that the series of alkaline and alkaline earthy uranates was chosen for investigation; for, the general formula of the salts being the same, the actual amount of uranium present in each molecule of the compounds is the same, though the density, and therefore the molecular weight and percentage amount of uranium, differ in the various salts. This is seen in Table II.

TABLE II.

Formula.	Molecular weight.	Per cent. of Uranium from Formula.	Per cent. of Base from Formula.	Electroscopic leak in presence of substance.		Atomic weight of Base.
				Unheated.	Heated.	
$U_2O_7Li_2$ ...	606	79·2	2·3	143	158	Li = 7
$U_2O_7(NH_4)_2$	628	76·4	5·7	125	171	NH_4 = 18
$U_2O_7Na_2$ ...	638	75·2	7·2	141	154	Na = 23
$U_2O_7K_2$ ...	670	71·6	11·7	137	132	K = 39
U_2O_7Ca ...	632	76·0(71·4)	6·3(11·9)	126	130	Ca = 40
U_2O_7Sr ...	679	70·7(62·7)	12·8(22·7)	117	121	Sr = 87
U_2O_7Ba ...	729	65·8(55·4)	18·8(31·6)	127	128	Ba = 137
$U_2O_7Tl_2$ ...	1,000	48	40·8	101	114	Tl = 204

Before proceeding to a detailed examination of the above table it must be noted that barium uranate, from whatever point of view considered, occupies an anomalous position so far as the rate of electroscopic leak in its presence is concerned. Two different specimens of barium oxide were used for the preparation of many samples of the uranate, but in all instances it was found that the rate of leak in the presence of barium uranate was faster than in the case of strontium uranate. Similarly, two specimens of strontium oxide were used for the preparation of many samples of strontium uranate with the idea that the fault might lie in this base, but the result was always the same. No suggestion is offered as to the reason for this discrepancy beyond the close relationship between barium and radium so far as concerns the preparation of the latter material.

Subject to the above exception (and to that of ammonium uranate, which will be considered later) it is clear from the table that the rates of electroscopic leak in the presence of the various uranates diminish as the atomic weight of the base present in the uranate increases. Moreover superficial examination indicates that a better comparison can be instituted in this direction than in that of the different percentages of uranium in the various compounds. Thus, the percentage amounts of uranium in the strontium and potassium uranates are approximately the same, but a considerable difference exists between the rates of electroscopic leak in their presence, while the calcium and ammonium salts, which have a higher percentage of uranium than either of them, occupy an intermediate position in respect of electroscopic leak.

Similarly, when considering the percentages of base in the various uranates, discrepancies are seen to be present. Thus the percentages of calcium, of sodium, and of ammonium are approximately the same, and yet the rates of leak are widely different; while the potassium salt, which contains a greater percentage of base than any of them, leads to an electroscopic leak which is intermediate in rate.

On considering the leaks in the presence of the strongly heated substances given in Table I. (and owing to the possibility that the small excess of alkaline oxide present alongside the uranate may absorb water, it is probable that the results obtained with them are more accurate) it is further seen that the rates of leak in the presence of the calcium and potassium uranates are practically identical. This observation raised the question whether the uranates of the alkaline earths possess the formulæ commonly assigned to them. Owing to the fact that doubling the amounts of the alkaline earthy constituents in the respective uranates yielded percentages (given in brackets in Table II.) which made a perfect series in which the amount of base present in the uranate varied inversely as the rate of leak with the substance in the electroscope, it was thought that the formula for barium uranate, for example, might be $U_2O_7Ba_2$ and not U_2O_7Ba. Quantitative estimation, however, showed that the latter formula is correct. It appeared, therefore, that in respect of their restraining influence upon the electrical property of uranium the alkaline earths act as diads.

But if the alkaline earth bases are to be assumed to act in a diad capacity in the molecule so far as their influence on the radio-active force of the uranium is concerned the same property should be exercised by the oxygen atom. Similarly the nitrogen and sulphur atoms in the nitrate and sulphate of uranium respectively and the nitrogen in the ammonium uranate should give evidence of their individual valencies. It follows, further, if the rate of discharge of the electroscope in the presence of a uranium compound varies inversely with the atomic weight and valency of the atoms other than uranium, that the product of the rate of leak and the value representing the molecular weight and valency (V.M.W.) of the elements composing that uranium compound must be a constant for all uranium compounds examined under identical electroscopic conditions. And lastly, if these assumptions be true in the case of uranium, they should also be true in the case of thorium compounds.

In Table III. a series of values has been given in which the two factors, atomic weight and valency of the constituent atoms (other than the radio-active) of the molecule of the compound, are taken into account, and these. in the fourth column, have been multiplied by the corresponding rate of leak ascertained by experiment. The U and Th atoms in the compounds have been assigned their atomic weights alone, their valencies being left out of account. The radio-activity manifested by the U or Th atom may be regarded as its *surplus* energy, and therefore cannot act upon the atom which produces it. On the other hand the mass (apart from radio-activity) enters into the composition of the molecule of the compound, and consequently the atomic weight of the U or Th must be included in the valency-molecular weight.

TABLE III.

Table showing that the product of the valency-molecular weight and the rate of electroscopic leak is a constant for all compounds of (a) *uranium.* (b) *thorium.*

Formula.	Valency-molecular weight. (V.M.W.)	Mean rate of leak in presence of compound.	Product of V.M.W. and leak = constant.
$\frac{U_2O_5}{2}$	$320 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_5}{2}\times 2 & = 80\end{array}\right\}$	175	56000
$\frac{U_2O_7Li_2}{2}$	$359 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{Li_2}{2}\times 1 & = 7\end{array}\right\}$	143	51337
$\frac{U_2O_7Na_2}{2}$	$375 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{Na_2}{2}\times 1 & = 23\end{array}\right\}$	141	52875
$\frac{U_2O_7K_2}{2}$	$391 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{K_2}{2}\times 1 & = 39\end{array}\right\}$	137	53567
$\frac{U_2O_7Ca}{2}$	$392 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{Ca}{2}\times 2 & = 40\end{array}\right\}$	126	49392
$\frac{U_2O_7(NH_4)_2}{2}$	$426 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{N_2}{2}\times 5 & = 70\\ \frac{H_8}{2}\times 1 & = 4\end{array}\right\}$	125	53250
$\frac{U_2O_7Sr}{2}$	$439 \left\{\begin{array}{lr}\frac{U_2}{2} & = 240\\ \frac{O_7}{2}\times 2 & = 112\\ \frac{Sr}{2}\times 2 & = 87\end{array}\right\}$	117	51363

TABLE III—*cont.*

Formula.	Valency-molecular weight. (V.M.W.)	Mean rate of leak in presence of compound.	Product of V.M.W. and leak = constant.
$\frac{U_2O_7Ba}{2}$	$489 \left\{\begin{array}{lcr} \frac{U_2}{2} & = & 240 \\ \frac{O_7}{2}\times 2 & = & 112 \\ \frac{Ba}{2}\times 2 & = & 137 \end{array}\right\}$	121	59169
$\frac{U_2O_7Tl_2}{2}$	$556 \left\{\begin{array}{lcr} \frac{U_2}{2} & = & 240 \\ \frac{O_7}{2}\times 2 & = & 112 \\ \frac{Tl_2}{2}\times 1 & = & 204 \end{array}\right\}$	101	56156
$UO_2(SO_4)$	$624 \left\{\begin{array}{lcr} U & = & 240 \\ O_2\times 2 & = & 64 \\ S\times 6 & = & 192 \\ O_4\times 2 & = & 128 \end{array}\right\}$	91	56784
$UO_2(NO_3)_2$	$636 \left\{\begin{array}{lcr} U & = & 240 \\ O_2\times 2 & = & 64 \\ N_2\times 5 & = & 140 \\ O_6\times 2 & = & 192 \end{array}\right\}$	80	50280
$U(SO_4)_2$	$880 \left\{\begin{array}{lcr} U & = & 240 \\ S_2\times 6 & = & 384 \\ O_8\times 2 & = & 256 \end{array}\right\}$	64	56320
ThO_2	$296 \left\{\begin{array}{lcr} Th & = & 232 \\ O_2\times 2 & = & 64 \end{array}\right\}$	173	51208
$Th(SO_4)_2$	$872 \left\{\begin{array}{lcr} Th & = & 232 \\ S_2\times 6 & = & 384 \\ O_8\times 2 & = & 256 \end{array}\right\}$	62	54064
$Th(NO_3)_4$	$896 \left\{\begin{array}{lcr} Th & = & 232 \\ N_4\times 5 & = & 280 \\ O_{12}\times 2 & = & 384 \end{array}\right\}$	58	51986

NOTE.—All the above specimens of uranium and of thorium compounds were made from a single stock of uranium oxide or thorium hydroxide in each case freshly prepared. It is probably accidental that the constants for the uranium and thorium series are so nearly identical. Variations in the case of uranium series are comparatively small in our experience (three different stock samples of uranium nitrate obtained at different times from the same manufacturer), but variations in the case of thorium series are much wider. Nevertheless, for compounds made from a single stock of hydroxide and prepared on one day—as in the example given in the table—a constant is always obtained by multiplying the V.M.W. into the rate of leak.

The importance of the valency of the individual atoms in arriving at the relative molecular weights in the present connection is well seen by comparing the nitrates and sulphates of uranium and thorium. There is no doubt that the electroscopic leak is faster when uranyl or thorium sulphate is present than when an equal area of the corresponding nitrate is present, and that in the case of uranous sulphate the rate of leak is slower than with either uranyl sulphate or nitrate. In Table IV. are set (A) the simple molecular weights; (B) the valency-molecular weights of the sulphates, S being regarded (i) as a diad, (ii) as a hexad; (C) the valency-molecular weights of the nitrates, N being regarded (i) as a triad, (ii) as a pentad; and (D) the valency-molecular weights in which the SO_4 and NO_3 have been regarded as divalent and monovalent groups.

TABLE IV.

Substance.	A. Simple Molecular Weight.	B. Valency-molecular Weight Atoms considered separately.		C. Valency-molecular Weight Atoms considered separately.		D. Valency-molecular Weight (SO_4) and (NO_3) considered as Divalent and Monovalent Groups.
		S diad.	S hexad.	N triad.	N pentad.	
$UO_2(SO_4)$	368	496	624		—	496
$U(SO_4)_2$	432	624	880	—	—	624
$Th(SO_4)_2$	424	616	872	—	—	616
$UO_2(NO_3)_2$	396	—	—	570	636	428
$Th(NO_3)_4$	480	—	—	784	896	480

It is clear from a comparison of the simple molecular weights of these substances and of thallium uranate with the rates of electroscopic leak in their presence, that a progressive series cannot be formed on the basis of simple molecular weights. It is true that the series in Table IV. indicates that uranyl and thorium sulphates should be accompanied by a more rapid leak than the corresponding nitrates, and that uranous sulphate should occupy the lowest place so far as the uranium sulphates and nitrate are concerned. But the mean leak with thallium uranate (having a simple molecular weight of 500 corresponding to one atom of uranium) is 101, while the mean leak with uranium nitrate and sulphates, which have far lower molecular weights, is universally lower than 101.

Similarly S cannot be a diad, for then uranyl sulphate should lead to a more rapid leak than thallium uranate, whereas the converse is the case. Nor can S be a hexad and N a triad, for then the uranyl sulphate should cause a less rapid leak than the nitrate, whereas the converse is the case. And in the last place it is impossible for the SO_4 to be regarded as a group and divalent, and for the NO_3 to be regarded as a group and monovalent, for such a view would be opposed to the fact that the leak in the presence of uranyl and thorium sulphates is more rapid than in the presence of the corresponding nitrates. It therefore appears that the only values which will satisfy the ascertained relative rates of leak of the five salts under consideration both in regard to themselves and to other compounds of uranium (and thorium) are valency-molecular weights in which N is regarded as a pentad and S as a hexad.

But perhaps the most convincing proof that valency of the atoms in a uranium compound, even though they constitute a group, is of fundamental importance in determining the rate of leak in the presence of that compound is afforded by a comparison of the behaviour of ammonium uranate with the other uranates of the alkalis and alkaline earths. On ordinary chemical grounds the NH_4 group should be regarded as monovalent, and as having a molecular weight of 18, this uranate therefore coming between those of lithium and sodium, and, in particular, causing the electroscopic leak to be more rapid than when sodium uranate is present. But a large number of experiments with different samples of uranates of sodium and ammonium (each pair being made from the same specimen of uranium nitrate) have shown without exception that the rate of leak in the presence of ammonium uranate is lower than in the presence of sodium uranate. Now the V.M.W. of $\frac{U_2O_7(NH_4)_2}{2}$, if (NH_4) be regarded as a monovalent group with molecular weight 18, is 370, which multiplied by the leak (125) yields a "constant" of 46250. If, on the other hand, the atoms of the NH_4 group be regarded severally so far as valency and atomic weight are concerned (N being regarded as a pentad), the V.M.W. of the compound becomes 426, which, multiplied by 125 gives 53250, a constant well according with those yielded by the other compounds of uranium, and particularly those yielded by the uranates. Further, the V.M.W. of 426 indicates that the rate of leak with ammonium uranate should be less than with either the potassium or calcium salts, and greater than with the strontium or barium salts. Allowing for the fact, mentioned above, that barium uranate has always held an anomalous position in the series, these conditions are fulfilled. Lastly, it is noteworthy (1) that in respect of their influence on the radio-activity of the uranium with which they are in combination, the basic radicle NH_4 and the acid radicles NO_3 and SO_4 are absolutely comparable and act by virtue of the valencies and atomic weights of the elements of which they are composed; and (2) that there is no variation in valency of the N or S atom throughout the entire series of compounds containing these elements, N being always pentad, and S always hexad.

The Effect of Incineration.—Evidence has been given above that the leak of an electroscope in the presence of a radio-active compound depends not only upon the presence of the radio-active element, but also is modified fundamentally by the atomic weight and valencies of the elements with which it is bound up in the molecule of that compound. So far as concerns the influence of atoms other than the radio-active, this fact can be shown in another and very striking way.

Apart from the opinion now generally held that the precipitate resulting from the addition of a solution of a heavy metal to an albuminous solution is a chemical compound or "albuminate" of the metal, and has a fairly constant composition, such a conclusion is suggested by the fact that seven different specimens of uranium-egg-white yielded respectively 9·6, 9·12, 10·2, 8·22, 10·2, 9·0, and 9·4 per cent. of uranium on quantitative estimation. Moreover, from such a compound, acetone, which is a ready solvent for uranium nitrate, fails to extract uranium except in traces. The uranium-pleural-fluid compound, similarly, yielded 9·84 per cent. uranium on quantitative estimation. Now the albuminous compounds of uranium, the nitrate, the sulphates and ammonium uranate differ from all the other compounds of uranium that have been examined in respect of the effect of strong heating. Whereas the one group undergoes a more or less complete disintegration of the molecule on strong heating the other is relatively unchanged. As will be seen from Table I., the small increase in rate of leak produced by heating a thermostable uranate or oxide is represented by an enormous rise in leak in the presence of the ash of a thermolabile uranium compound. Similarly a fundamental difference obtains between the thermostable thorium oxide and the thermolabile nitrate, sulphate, and the egg-white compound when the leak is examined before and after strongly heating the substance.

In Table V. are set the results of a single experiment showing the effects of incineration. The uranium compounds were prepared from a common stock of oxide derived from the stock of uranium nitrate, and the nitrate used in the experiment was freshly prepared from this oxide. Similarly the thorium compounds were prepared from a common stock of hydroxide that had been prepared from the nitrate on the day of experiment, and had been evaporated to dryness. So far as possible, therefore, the compounds of each substance are comparable amongst themselves.

TABLE V.

To show the Effect of Incineration of certain Inorganic and Organic Radio-active Compounds upon the Electroscopic Leak in their presence.

Substance.	Observed Electroscopic Leak per hour in presence of Substance.	
	A. Natural condition.	B. Incinerated.
$U(SO_4)_2$	64	138
$UO_2(SO_4)$	92	180
$UO_2(NO_3)_2$	80	187
Uranium-egg-white	12	133
Uranium oxide (yellow) used for preparing above	126	157
$Th(SO_4)_2$	62	124
$Th(NO_3)_4$	55	138
Thorium-egg-white	7·5	41·4
Thorium hydroxide used for preparing above ...	82	111

During Uranium experiments natural leak of electroscope 7·3 per hour.

During Thorium experiments natural leak varied from 7·3 (at commencement) to 14 (at end) per hour.

That this rise in leak is not due to the introduction of an actually greater amount of uranium or thorium into the electroscope, as might be the case if the thermolabile compound were incinerated in a different vessel, is proved by using a platinum instead of an aluminium dish for holding the material within the electroscope. Under these conditions the same material which has been examined for its effect upon the leak in the natural state can be incinerated, and, after cooling, the platinum dish can be replaced within the electroscope. This was the course actually adopted in all the experiments in which incineration played a part. It is possible that some part of the rise in rate of leak after incineration of an albuminate, for example, depends upon the fact that, now, relatively small molecules of uranium or thorium compound occupy the positions formerly occupied by the enormous albuminous portion of the unheated compound. For it is practically certain that a square centimetre of uranium or thorium albuminate must contain fewer molecules than the same extent of uranium or thorium oxide, and on incineration the former positions of protein may become occupied by uranium or thorium oxide set free from albuminate molecules of superincumbent layers. But that this is not the entire explanation is rendered probable by the facts (1) that a great rise in rate of leak is not eliminated by incinerating the thinnest possible layer of albuminate, and (2) that incineration of thorium nitrate is not accompanied by a diminution in volume, but, on the contrary, by a considerable increase. Moreover, whether the molecules of the thermostable uranates be of the same size whatever the base with which the uranium is linked or not, there is no doubt that the densities of the molecules increase proportionately to the atomic weights of the bases. Hence it is not unreasonable to suppose that the density of the albuminous molecule, as distinguished from its size, plays some part in the production of the low radio-activity of the uranium or thorium albuminate.

The Character of the Radiations concerned in the Production of the Electroscopic Leak in the presence of the Uranium and Thorium Compounds.—On the assumption that aluminium foil excludes α-radiations and allows the β and γ-rays to pass through it is possible to subdivide the leak obtained in the case of the various compounds both before and after incineration and come to a conclusion as to the particular variety of radiation concerned. By subtracting the leak per hour with the substance covered from the leak per hour with the substance uncovered the portion of the total leak due to α-particles is given, any effect due to β-radiations of extremely low penetration being neglected. This has been done in the following Table :—

TABLE VI.

Substance.	Natural Condition. Portion of Rate of Leak per hour due to		Incinerated. Portion of Rate of Leak per hour due to	
	α-rays.	**β** and γ-rays.	α-rays.	**β** and γ-rays.
$U_2O_7Li_2$	113	30	132·1	25·9
$U_2O_7Na_2$	103	38	123·5	30·5
$U_2O_7K_2$	104·7	32·3	107·5	24·5
U_2O_7Ca	96	30	104·0	26·0
$U_2O_7(NH_4)_2$	101·2	23·8	145·5	25·5
U_2O_7Sr	91·5	25·5	100·8	20·2
U_2O_7Ba	93·6	27·4	103·6	24·4
$U_2O_7Tl_2$	79·4	21·6	82·6	21·4
$UO_2(SO_4)$	57	35	142·8	37·2
$UO_2(NO_3)_2$	52·4	27·6	151·9	35·1
$U(SO_4)_2$	52·8	11·2	127·0	11·0
Uranium-egg-white ...	4·8 *	0·6 *	124·0	1·8 *
U_2O_5 (black)	145·8	29·2	144·0	33·0
$Th(SO_4)_2$	24·1	77·9	78·4	27·6
$Th(NO_3)_4$	21·7	70·6	127·8	16·2
$Th(OH)_4$	104·0	496·0	123·0	22·0
Thorium-egg-white ...	3·1 *	1·4 *	46·5	7·8 *

* In the case of these low values the ascertained leak has been corrected by the natural leak of the electroscope determined specifically for the purpose on each occasion. In the case of more rapid leak the natural leak has been neglected. All the thorium compounds were prepared one day, and electrically examined the next.

In addition to the points which have been referred to previously, the Table shows that the amount of α-rays diminishes as the valency-molecular weight increases. In the case of the thermostable uranium compounds the fact is even better seen when the substances have been strongly heated. So far as concerns the β and γ-rays a difference appears between the unheated and strongly heated substances. In the natural state the β and γ-rays like the α seem to diminish in amount as the molecular weight of the compound increases, but in the strongly heated thermostable compounds the amount of β and γ-rays appears to be fairly constant. Differences in either direction are, however, slight, and it is not possible to speak with certainty. Nevertheless it is clear from the behaviour of the thorium compounds that incineration may drive off a material which is accountable for an enormous amount of β and γ-rays.

But the most striking fact shown by the series is that incineration sets free a large number of α-rays. Indeed, it is to these almost entirely that the great increase in leak seen upon incineration of the thermolabile uranium and thorium compounds is due.

An interesting point is shown by the particular series of thorium compounds that is given in this Table. When examined uncovered the incinerated sulphate showed only a slight rise in leak over the unheated, the incinerated nitrate showed a considerable rise, and the incinerated hydroxide showed an enormous *decrease.* It was only when the radiations were considered separately that the explanation was apparent. When this was done the thorium series fell completely into line with that of uranium.

Compounds of uranium and of thorium with egg-white.—The electrical behaviour of compounds of thorium and of uranium with egg-white and other albuminous substances is of great theoretical importance. Although quantitative estimation of the amount of thorium in the compound does not give so satisfactory information concerning the available amount of radio-activity as does quantitative estimation of the amount of uranium owing to the great radio-active variability of thorium, the fact remains that combinations of uranium with egg-white, in which the radio-active element is present to the amount of 8–10 per cent., and in which, after incineration, the presence of active radio-active material in large amount is demonstrable, yield very small electrical evidence of radio-activity. As will be seen later, such compounds may be entirely without effect on photographic plates. Molecules or combinations of molecules of such a size are easily to be imagined which in combination with a radio-active substance would produce a "radio-active compound" yielding in the natural state neither electrical nor photographic evidence of radio-activity. The same is true for thorium albuminates, at least directly after their preparation, provided that a hydroxide free from thorium-X be used in their preparation.

Uranium Mixtures compared with Uranium Compounds.—Water of Crystallisation.—The admixture of molecules containing no radio-active factor does not affect the rate of leak in the same way as the non-radio-active atoms in a radio-active compound affect the radio-active atom. This is shown by the following experiment.

If from a given sample of uranium nitrate the rate of leak of which is 80 per hour an ammonium uranate be made by adding ammonia, and this be subsequently re-dissolved in nitric acid and evaporated to dryness, a mixture of uranium and ammonium nitrates will be produced as in the formula $U_2O_7(NH_4)_2 + 6HNO_3 = 2UO_2(NO_3)_2 + 2NH_4NO_3 + 3H_2O$.

Now the rate of leak of this mixture of nitrates is 69 per hour, and on the basis of simple molecular weights its composition is 396 uranium nitrate with 80 ammonium nitrate, and $\frac{396}{476} \times 80$ (rate of leak of uranium nitrate) $= 67$. On the other hand if it were assumed that a compound uranio-ammonium nitrate was formed the valency-molecular weight would be 876, and this (taking the constant as 55000) would indicate a leak of 63 per hour.

It is probable that water of crystallisation is to be regarded rather as an admixture than as entering into the composition of the radio-active compound in the present connection. The amounts of water of crystallisation have been carefully estimated in the case of the nitrates and sulphates of thorium and uranyl. It was found that the formulæ of the salts corresponded closely at the time of examination with the following:—$UO_2(NO_3)_2 . 6H_2O$, $Th(NO_3)_4 . 3H_2O$, $UO_2(SO_4) . 4H_2O$, and $Th(SO_4)_2 . 8H_2O$. Upon the assumption that the water molecules enter into the composition of the radio-active compound, the valency-molecular weights (N being pentad and S hexad) become 840 for $UO_2(NO_3)_2 . 6H_2O$, 760 for $UO_2 (SO_4) . 4H_2O$, 990 for $Th(NO_3)_4 . 3H_2O$, and 1144 for $Th(SO_4)_2 . 8H_2O$. These values satisfy the relative rates for the leaks of the uranium salts, but are opposed to the fact that the leak with thorium sulphate is more rapid than with the nitrate. Moreover all fail in respect of the constant produced by multiplying the V.M.W. into the corresponding rate of leak. On the other hand, if the molecules of water of crystallisation be regarded as an admixture like the molecules of ammonium nitrate in the experiment described above, the observed rates of leak require correction for the varying amounts of water of crystallisation. In regard to this correction valency plays no part, but simple molecular weights alone are concerned. These corrections indicate that the rate of leak for water-free uranyl nitrate is 102, for water-free uranyl sulphate 110, for water-free thorium nitrate 61, and for water-free thorium sulphate 83, per hour. Such values are quite in accord with the indications afforded by the relative valency-molecular weights of the sulphates and nitrates, and lead to constants not far removed from those obtained in the case of the incinerated thermostable uranates, from which it is certain that water must practically be absent.

The Photographic Results.—This part of the research can be dismissed shortly. In the case of none of the uranium or thorium-egg-white compounds, if examined within a few days of their preparation, was an effect produced on a photographic plate through mica, though plate and substance were kept in relation for 18 hours at a temperature of 55° C. A possible exception to this statement occurred in the case of a few of the thorium-egg-white compounds. None of the uranium-egg-white compounds affected a photographic plate under the same conditions of time and temperature when the substance and plate were separated only by a layer of air one millimetre in depth. Under similar conditions a few of the thorium-egg-white compounds showed a slight direct effect, but the majority were without effect. Uranium-serum and uranium Witte's peptone were similarly without effect upon the plate both as concerns direct action and action through a mica screen. Of compounds of uranium and spleen pulp no specimen showed action through mica, and only such specimens produced a direct effect as were made from samples of spleen which showed a direct action without any admixture of uranium. If anything, in such cases the uranium compound showed a slighter effect upon the plate than the uranium-free substance.

If some months be allowed to elapse between the time of their preparation and their photographic examination the results are somewhat different. Under these circumstances all the uranium albuminous compounds were found to affect the plate both when separated from it by 1 mm. of air and when separated from it by paper that had been brushed over with egg-white. The thorium albuminous compounds on the other hand did not act on the photographic film through egg-white paper, and not all of them affected it when separated from it by a layer of air only.

The ash of the uranium and thorium-egg-white compounds after incineration was, without exception, without action on a photographic plate through mica, and the position of the ash was indicated by a clear spot on the somewhat fogged plate; when acting through one millimetre of air it led to deposition of silver on the plate.

The uranates and the sulphates and nitrate of uranium produced definite effects upon the photographic plate both directly and through mica. Though leading to a greater effect when only separated from the plate by air, and though the effect of the incinerated material appeared to be slightly greater than that of the unheated, the relative effects shown by the various compounds were the same through air as through mica. Thus the uranium sulphates caused a greater deposition of silver than the nitrate. The greatest photographic effects were shown by the sulphates of uranium and the uranates of sodium, potassium, and calcium, the least effect by the nitrate, and intermediate effects by the other substances. These results are well in accordance with the relative amounts of β and γ-rays emitted by the various substances as indicated in Table VI. (p. 171).

CONCLUSIONS.

From the preceding experiments we draw the following conclusions :—

1. A distinction must be drawn between recognisable and latent (or unmasked and masked) radio-activity.

2. The latent radio-activity of thermolabile compounds may be set free by incineration.

3. The latent radio-activity consists chiefly, if not entirely, of α-particles.

4. In the case of a series of compounds containing the same amount of either uranium or thorium in the molecule the unmasked radio-activity as evidenced by its influence on electroscopic leak, and to a less extent by its effect on a photographic plate, varies inversely as the valency and atomic weight of the atoms other than the radio-active with which the uranium or thorium is combined.

5. The product of the valency-molecular weight and the rate of leak under identical conditions is a constant for all compounds of a uranium or thorium series.

6. In respect of their influence upon the radio-activity of a uranium or thorium atom with which they are combined, the acid radicles NO_3 and SO_4 and the basic radicle NH_4 act by virtue of the atomic weights and valencies of the individual atoms of which those radicles are composed, and do not act as monovalent or divalent groups.

7. In a mixture of a uranium and a non-radio-active compound the valencies of the atoms of the non-radio-active compound play no part in determining the rate of electroscopic leak of the radio-active compound

8. So far as concerns its influence upon the rate of leak, water of crystallisation in a uranium or thorium compound is comparable with a mixture of water molecules and molecules of the radio-active compound, and is not to be regarded as a fundamental constituent group of the radio-active compound.

9. Compounds of uranium and thorium with egg-white and other albuminous substances, though they contain about 10 per cent. of the radio-active element, lead to the production of radio-active compounds from which all photographic evidence of radio-activity may be absent, and of which the effect on electroscopic leak is slight. After incineration the ash yields marked electrical effects and moderate photographic effects through a thin layer of air; no photographic effect is produced when the ash is separated from the photographic plate by a thin sheet of mica.

PRELIMINARY COMMUNICATION ON THE POWER OF CERTAIN MICRO-ORGANISMS TO AFFECT A PHOTOGRAPHIC PLATE IN THE DARK.

By H. MacCORMAC.

It has been shown by Dr. Russell and Dr. Lazarus-Barlow that certain woods and certain animal tissues, respectively act on a photographic plate in the dark, no evidence of this activity being apparent before development of the negative.

At the suggestion of Dr. Lazarus-Barlow the action of micro-organisms towards a photographic plate under such conditions was investigated.

Method.—On the first trial, Koch's plates were made with agar, and on the surface parallel lines of *Staphylococcus aureus* were inseminated. These were incubated, when a good growth took place, and then put into a light-tight box, face to face with the film of a photographic plate,* but separated from it by a cotton thread, tied across each end of the plate. The plates were wrapped in paraffined paper and exposed for 18 hours at 50° C.

When the plate was developed, it was found that the agar had caused a heavy shadow, relieved by light lines marking the position of the bacterial growth. As agar was able to produce such an effect, this method could not be used.

Next, agar sloped tubes were inoculated with *Staphylococcus pyogenes aureus*, and a good growth was obtained; this was scraped off with a platinum loop, emulsified in distilled water, and painted on clean glass plates with a sterilized camel's-hair brush. It had previously been determined that the surface scrapings and condensation water from a sterile tube were inactive. Fairly satisfactory results were got in this way, but it was found more convenient to substitute for the brush a glass tube drawn to a fine capillary point, forming a kind of stylographic pen, the bacterical emulsion taking the place of ink. With this, the name of the germ used could be written on clean glass, thus making more easy identification of the shadow-producing organisms.

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* "Imperial Special Rapid" plates were used throughout this research

General.—Twenty-seven different micro-organisms were tested, and the results obtained are set forth in the accompanying table.

Name of organism.	Number of times tested.	Number of positive results.	Depth of "shadow" on photo-plate	Corresponding value on Benoist gauge.*
B. of Rabinowitch	1	0	None	0
Baker's Yeast	2	2	Very faint	1
B. Cohn I	4	0	None	0
Sarc. flava	5	1	Medium	3
B. Flexner	3	1	Very faint	1
B. Gärtner	1	0	None	0
B. tuberculosis (dry)	3	2	Good	4
M. neoformans	1	1	Good	4
B. phosphor. albiensis	2	0	None	0
B. v. Metchnikoff	1	1	Very faint	1
B. diphtheriæ	3	3	Medium	3
B. Hoffmann	1	1	Faint	2
B. intest. sporogenes	6	0	None	0
B. megaterium	10	2	Good	4
B. coli	9	1 (?)	Very faint	1
V. choleræ	7	0	None	0
B. Danysz	5	0	None	0
M. citreus agilis	6	1	Medium	3
Staph. pyog. aureus	19	18	Strong	5
Staph. pyog. albus	5	4	Strong	5
B. phleii II	6	3	Faint	2
B. prodigiosus	8	4	Medium	3
B. typhosus	6	2	Faint	2
B. tuberculosis (bovine)	3	2	Strong	5
B. pyocyaneus	7	1	Faint	2
Throat yeast (pathogenic)	7	4	Medium	3
B. mycoides	1	0	None	0

* Arch. Midd. Hosp. Vol. XIII., 1908, Seventh Cancer Report, p. 112.

Attempts were made to deal with streptococci and pneumococci, and it was hoped, with these, to test virulent against avirulent forms, this property being modified by subculture and passage through animals. Unfortunately from a growth so slight no sufficient quantity could be obtained.

Several points arise out of these findings. In the first place, it is evident that every organism is not capable of producing an effect: and it is further evident that some produce results regularly; others are more fickle, now positive, again negative; while others cannot affect a photographic plate at all.

The effect certainly varies in proportion to the amount of material used, but the differences must be considerable before any change can be appreciated. This is shown by the following. A very thick emulsion was made from *Staphylococcus pyogenes aureus;* this was diluted 1 in 2, 1 in 8, and 1 in 64. Exactly equal quantities were measured from the original and from the diluted emulsions in a fine tube: these were spread on coverslips of equal area. All four were exposed to the same plate, and the resulting "shadows" compared by means of a radiogram taken through a Benoist gauge.

The primary emulsion gave a shadow equal to 4 on this scale; the dilution of 1 in 2 gave a shadow equal to 3; the dilution of 1 in 8 gave a shadow equal to 2; the dilution of 1 in 64 gave no appreciable shadow.

Now it was noticed, when making the emulsions from different bacteria, that although quantities seemingly equal were used, different bacteria formed emulsions of very different opacity. Thus, when dried, *B. coli* formed on glass a film so meagre that if it were placed even on a dark background it could scarcely be seen. As this organism but once—and that was doubtful—gave any result out of 9 trials, it might seem this explained its inactivity. Such, however, is not the case, for both *B. prodigiosus* and *B. phleii II*, making films of an opacity quite as poor, were fairly active. Further, other organisms, giving an emulsion of comparative thickness, were very inactive.

In this connexion it was at first noted that *B. megaterium*, forming a dense film, was invariably negative. When, however, young cultures in which little sporing had taken place were used, a good "shadow" could be got. The formation of pigment appears not to influence a result. If *B. prodigiosus* be grown at 37° C. and at room temperature, a similar "shadow" is obtained, although the former growth is free from visible colour.

To test how far the amount of substance used determines the result, sub-cultures were made from different organisms.

From each tube, ·008 gram was taken, emulsified with distilled water, and spread on covers of equal area. Below a table indicating the results is given.

Name of organism.	Result.	State of emulsion and film made from it.
B. phosph. alb.	No shadow	Thin
Sarc. flava	,, ,,	Good
Throat yeast	Good shadow	Good
B. prodigiosus	Faint ,,	Thin
B. pyocyaneus	,, ,,	Thin
B. diphtheriæ	,, ,,	Good
B. mycoides	No ,,	Good
B. megaterium	,, ,,	Good
V. choleræ	,, ,,	Thin
M. cit. ag.	,, ,,	Medium
B. paratyphosus (a)	,, ,,	Poor
,, ,, (b)	,, ,,	Medium

It would thus seem that a failure to act on a photographic film was not entirely the result of using too small quantities.

The following experiment was made to determine the distance at which the bacterial culture is capable of acting on the film. On each of 4 coverslips of equal area ·005 gram of *Staphylococcus pyogenes aureus* was spread; these coverslips were then exposed to the same photographic plate at distances of 1, 2, 3, and 4 mm. The result was as follows:—

When separated by 1 mm. a fair shadow appeared.

When separated by 2 mm. a scarcely preceptible shadow appeared.

When separated by 3 mm. and 4 mm. there was no result.

These findings suggested that the effective substance was possibly gaseous. To test this question, ·5 gram of dried tubercle bacilli, such as is used in opsonic work, was put in a glass tube of 5 mm. diameter drawn to a fine point, the lower end being plugged with cotton wool. This was arranged so that air coming through it impinged upon a photo-plate, and for 18 hours a steady current was passed. No shadow could be obtained, although the experiment was repeated several times.

As a cylinder of compressed air had been used, it seemed possible that the low temperature might be responsible for failure. The air was therefore heated by passage through a coiled tube immersed in water kept at 55° C. Under these conditions also the photographic plate showed no deposition of silver on development.

These same bacilli had given previously an excellent "shadow" when emulsified in the usual way.

CONCLUSION.

Certain micro-organisms, notably *Staphylococcus pyogenes aureus* and *albus*, *B. diphtheriæ*, *B. tuberculosis*, and a pathogenetic throat yeast, have the power of acting upon a photographic plate in the dark when exposed at a short distance from it for 18 hours at 55° C. This power is wanting in the case of many other micro-organisms, and is fickle in certain others. The substance which affects the plate apparently cannot be carried along with a stream of air, nor does it depend upon the pathogenicity or non-pathogenicity of the micro-organism.

The further characters of the property are under investigation.

ON GRANULES IN CELLS OF NORMAL TISSUES AND NEW GROWTHS.

By HENRY BECKTON.

I. INTRODUCTION.

In the "Journal of Pathology and Bacteriology" (Jan. 1909), using a method there given in full detail, I have described granules in certain types of human cell occurring in tissues removed at operations and at post-mortem examinations. The granules found in glandular structures (liver, submaxillary gland, columnar epithelium of intestine) resembled those described by Altmann in the corresponding structures of lower vertebrates, while the granules of plasma-cells and lymphocytes agreed in the main with those described by Schridde. Granules were also described in endothelial cells and fibroblasts.

During the research examination was made of nine cases of new growth, seven of which were malignant and two non-malignant, and it appeared that the malignant neoplastic cells were devoid of granules, while they were present in the cells of the non-malignant growths. This observation has been made the subject of further investigation, the results of which form the main part of the following communication.

II. METHOD OF INVESTIGATION.

Full details of the method are given elsewhere (*loc. cit.*). It is only necessary to state here that it is, briefly, as follows: Fixation of tissues in formol-Müller (1 : 49) followed by simple Müller, embedding in paraffin, staining with Altmann's anilin acid-fuchsin and differentiation with picric-acid alcohol. Subsequent experience has shown that in many cases, though not in all, the length of fixation in formol-Müller may be abbreviated to three days, and subsequent treatment with simple Müller may be omitted. It has not been found safe, however, entirely to discard the older and longer treatment.

Similarly a period of three or four hours has been found sufficient for the washing of pieces of tissue half a millimetre in thickness.

With regard to the action of the fixing-fluid employed, it is to be noted that formalin by itself is sufficient for the demonstration, on staining, of both granules and nuclear detail in certain cells, *e.g.*, those of pancreas, liver, and submaxillary gland; in these cases granules are brought out not only by Altmann's anilin acid-fuchsin, but also by Muir's alcoholic eosin method. But for the demonstration of granules in certain other cell-species, *e.g.*, lymphocytes and plasma-cells, the potassium bichromate is the essential constituent in the formol-Müller solution; thus granules in these cells may be demonstrated after fixation with Müller's fluid alone, but not with formalin alone. This observation indicates both a difference of composition between the granules of different cell-species and a means of classifying cells and their granules in accordance with the micro-chemical reactions of the latter.

III. THE NORMAL TISSUES.

As a convenient standard of comparison in estimating the size of granules generally, those of eosinophil cells have been taken; these granules appear as bright red, highly refractile, spherical bodies of practically uniform size. The method indicates that eosinophil cells are far more commonly met with in tissues than is usually supposed.

The granules of some of the cells in the following tissues have been already described (*loc. cit.*), but their appearances are briefly recalled here for convenience of reference. In a few cases the material was of necessity obtained post mortem.

The Submaxillary Gland.—The granules are readily seen in a section stained by hæmatoxylin and eosin; with anilin acid-fuchsin followed by picric-acid alcohol they stand out sharply, their deep red colour contrasting strongly with the groundwork of the section. They show considerable variety in size, and are on an average larger than eosinophil granules; they are almost always round, but occasionally oval, in shape;

while their distribution is variable, depending on the state of activity of the cell; thus the whole cell-body may be crowded with granules, or only a few may be present near the lumen.

The Pancreas.—The cells of the pancreas contain granules similar in appearance to those of the submaxillary gland, but less variable in size.

The Liver.—After fixation of liver tissue by almost any method the cytoplasm of the liver-cells appears to be *granular*, though it cannot definitely be said to contain discrete granules. But on fixing as above and staining with anilin acid-fuchsin alone, or better still after subsequent differentiation with picric-acid alcohol, large round granules are to be seen of approximately the size of those in eosinophil cells, but showing a considerable variability in this respect. The granules may be numerous and distributed uniformly throughout the cell-body, or they may be fewer and scattered; these different appearances are influenced by the following factors at least—(*a*) the position of the cell in the lobule, (*b*) the amount of fatty change, (*c*) the presence of pigment-granules.

The Kidney.—A sharp distinction must be made between the cells of the secreting and those of the conducting portions of the organ. For as a rule a secreting cell is crowded with closely-set granules, having a radial arrangement from the base of the cell towards the lumen of the tubule. At first sight rods seem to be of frequent occurrence, but close examination resolves these into rows of granules or into beaded chains formed by the partial coalescence of a number of viscous spherical bodies. Not all alveoli of secreting cells, however, show these appearances. In different parts of a sufficiently large section varying numbers of such alveoli are found to contain few or even no granules in the bodies of their lining cells. But whereas the secreting cells are usually crammed with granules, they are almost wanting in the cells of the collecting tubules, and the difference is so great that in a section stained for granules it may become recognisable to the naked eye.

The Thyroid and Parathyroid.—The cells of the single layer of cubical epithelium lining the thyroid alveoli contain numerous granules which are smaller than those of eosinophil cells and are distributed throughout the whole cell-body.

The granules of the essential cells of parathyroid tissue are similar to those just described, but are less numerous.

Columnar Epithelium.—The columnar epithelium of the intestine contains minute granules distributed throughout the cell-body, with the exception of a narrow rim of protoplasm along the free margin ; in the basal portion of the cell they are very closely set, but between the nucleus and the free border they are more openly arranged. In cells containing a moderate-sized drop of mucus the basal portion of the cell may still be crowded with granules, while those in the immediate neighbourhood of the drop of mucus are fewer in number and may be somewhat larger than usual. In a cell which has become little more than a goblet of mucus with a nucleus lying against its edge surrounded perhaps by a small remnant of protoplasm, very few or no granules are present.

Granules have been demonstrated also in columnar epithelium occurring in situations other than the intestine, viz., in the endometrium, in the lining of the gall-bladder, and in the ducts of various glands. In all these cases the granules are very small, and a marked radial arrangement from the base of the cell towards the lumen is present in the cells lining small ducts.

Endothelial Cells and Fibroblasts.—When stained by ordinary methods these cells do not show granules, but with acid-fuchsin followed by picric-acid alcohol, after the special fixation, minute red dots are seen in the cell-protoplasm, particularly towards the ends of the oval nucleus; they nevertheless often occur irregularly distributed throughout the rest of the cell-body, and occasionally the granules are of considerable size.

Adipose Tissue.—The amount of protoplasm in the body of a fat-cell is very small, and the granule-appearances are inconspicuous. Nevertheless granules are present ; they are usually very small, and sometimes exceedingly minute, and exhibit no regular arrangement in the cell-protoplasm.

Lymphocytes.—Tissue-lymphocytes as observed in sections of lymphatic glands, tonsil, vermiform appendix, etc., as well as in the small-cell infiltration of chronic inflammatory processes, show in their scanty cell-protoplasm a patchy distribution of small round granules. Usually the diameter of these granules is about one half or one third that of an eosinophil granule, although occasionally their size is larger and may even approach that of the granules of eosinophil cells. Blood-lymphocytes appear to differ from tissue-lymphocytes, as far as granules are concerned, in containing more numerous but rather smaller granules, although it is often impossible to decide on granule-appearances alone whether a given cell is a tissue- or a blood-lymphocyte.

Plasma-cells (Unna).—Typically a plasma-cell presents the following appearances: The cell-body is oval or rounded, according to the plane of section, but may assume any other form in accordance with the space in which it lies; its greatest diameter is usually about twice that of its nucleus, when this is single; it sometimes shows a very characteristic "clear space" which is not a vacuole, but shades off gradually into the surrounding part; its cell-protoplasm is somewhat basophil in reaction. The nucleus is generally of about the same size as that of a lymphocyte, but is sometimes considerably larger; it is round or very nearly so, and is usually placed excentrically—often at the very end of an oval cell-body; it is characterised by the presence of a number of small masses of chromatin placed peripherally. Occasionally a plasma-cell contains two, rarely three or more, nuclei. In common with lymphocytes plasma-cells have special staining reactions which are well brought out by Unna's polychrome methylene-blue, by Pappenheim's methyl-green pyronin mixture, and by Bonney's stain.

The granules, which are usually a little smaller than those of eosinophil cells, tend to be aggregated around the nucleus, although sometimes they surround a "clear space" or a definite vacuole, or are arranged quite irregularly. They are generally round; rarely they are represented by small rods; and occasionally they appear as globules of considerable size. There is reason to believe that these large globules are produced by a coalescence of ordinary granules, which undergo at the same time some as yet undefined change of composition.

Squamous Epithelium.—Altmann-granules, as opposed to pigment- and keratohyalin-granules, are never found in squamous epithelium. To this statement one or two rare and only partial exceptions have been observed; in these cases minute granules were present in small numbers in the basal layer of the epidermis, and in this situation only.

Unstriped Muscle, etc.—In addition to the foregoing cells described as containing granules, certain others met with incidentally in the course of the present investigation, such as those of the sweat and lacrimal glands, and the cells of the stroma of the endometrium, have been observed to contain granules. Striped muscle shows lines and bands composed of dots and short rods respectively; unstriped muscle-fibres, on the other hand, are entirely devoid of granules, a point which serves to differentiate these cells from fibroblasts when the two cell-species are otherwise indistinguishable.

IV. INFLAMMATORY CONDITIONS.

In addition to cells containing eosinophil and basophil granules the chief cell-species here concerned are lymphocytes, plasma-cells, endothelial and endothelioid cells and fibroblasts. All these have been found to show Altmann-granules in every case investigated, including acute abscess, chronic mastitis, tuberculous disease, and other chronic inflammatory states; moreover, granules are well shown in the chronic inflammatory (or precarcinomatous) conditions seen at the edge of the new growth in many cases of carcinoma.

V. THE NEW GROWTHS.

The following description of granules in cells of new growths is based upon an examination of 45 cases the histological appearances of which are shown in the following list:—

A. Non-malignant New Growths.

Adenoma: Thyroid (5), Prostate (1).
Adenomyoma: Uterus (1).
Fibroadenoma: Breast (1).
Papilloma: Bladder (1).
Duct-papilloma: Breast (1).

B. New Growths of Doubtful Malignancy.

Neoplasms of Orbit (1), Ovary (1), Thyroid (1).

C. Malignant New Growths.

Carcinoma, spheroidal-cell: Breast (13), Pancreas * (1), Liver * (1).
Carcinoma, squamous-cell: Cervix Uteri (3), Anus (1), Skin (1), Lip (2), Tongue (2).
Carcinoma, columnar-cell: Corpus Uteri (2), Rectum (1).
Sarcoma, melanotic: Vulva (1).
Endothelioma: Breast (4).

Except in the two instances marked * all of the material examined was obtained after operation.

A. Non-Malignant New Growths.

1. Adenoma.—In the case of the thyroid four of the adenomata were of ordinary type, although in one of them the alveoli were separated from each other by an unusually large amount of colloid material. The granules in each case were of about the same size as in normal thyroid tissue, but much fewer in number. The remaining adenoma of the thyroid presented the appearances characteristic of exophthalmic goitre; the great majority of the alveoli were larger than normal, and in many of them a considerable degree of epithelial proliferation had taken place. Here the granules were much less numerous than in cells of normal type, as was also the case in alveoli showing a distinct transition from cubical to columnar epithelium, or simply a single layer of atypical epithelium; with the exception, however, that in a fairly large number of alveoli one or two cells were present resembling cells of normal type in containing numerous granules.

It is interesting to note here that in simple proliferation of lymphoid tissue, e.g. in hypertrophy of the tonsil, there appears to be no diminution in number of granules in the lymphocytes.

The adenoma of the prostate shows proliferation of the glandular elements which contain granules in moderate number, but it is not known whether these are the same in number as, or fewer than, in the normal prostate.

2. Adenomyoma.—In this case of new growth of the uterus a section shows comparatively few tubules derived from the endometrium embedded in a mass of unstriped muscle. The latter tissue shows no granules (v. supra), while in the columnar epithelium lining the tubules fewer granules are present than in that of the normal endometrium.

3. Fibro-adenoma.—An example of this form of new growth removed from the breast showed but few granules in the epithelial cells.

4. Papilloma.—A villous tumour removed from the bladder showed a stroma of connective-tissue arranged in processes covered with transitional epithelium, the cells of which contained many small granules and fine threads or chains of granules (cf. normal kidney). It may be noted that the granules of the epithelial cells were of a violet-red tint, those of the cells contained in the stroma being of a brick-red colour.

5. Duct Papilloma.—A small tumour excised from the breast showed in several of the ducts cut across in a section papilliform processes covered with columnar epithelium composed of large cells containing numerous round granules. These were for the most part of about the same size as eosinophil granules, but here and there they attained a much larger diameter.

B. New Growths of Doubtful Malignancy.

1. Orbit.—Histologically this case of new growth was diagnosed as a small round-cell sarcoma, but clinically it presented a very low degree of malignancy, since the total mass of growth was not more than about one cubic centimetre, and the history extended over several years. A section was seen microscopically to present the appearances of nodules of lymphoid tissue, and the cells composing this both as regards granules and in other respects closely resembled ordinary tissue-lymphocytes.

2. Ovary.—The new growth in this case was a papilliferous cystadenoma, in which most of the cells showed many small round granules.

3. Thyroid.—A section of the new growth in this instance showed extensive irregular proliferation of the epithelial cells, which contained almost or quite as many granules as most of the cells in the cases of the adenomata already described.

C. Malignant New Growths.

1. Spheroidal-cell Carcinoma.—In this group of cases of malignant disease either no granules have been found in the cancer cells, or they were present only in small numbers in few of them. This statement applies to metastases in the axillary lymphatic glands as well as to the primary growth itself. One notable exception was found, however, in which granules, although present only in a small number of the cancer cells, formed a very striking picture. They were variable in size, but on the whole about as large as eosinophil granules, and the granule-containing cells presented a remarkable distribution, occurring for the most part only in finger-like processes of new growth, or at the margins of rather larger cell-masses, but being almost entirely absent from the principal mass of new growth.

In the cases of primary carcinoma of the pancreas and of the liver examined, no positive results have been found, since the material was of necessity obtained post mortem.

2. Squamous-cell Carcinoma.—In no case of squamous-cell carcinoma have granules been found in the cancer cells.

3. Columnar-cell Carcinoma.—In the case of columnar-cell carcinoma of the rectum the great majority of the cells contained no granules. Here and there, however, a cancer cell, or small group of such cells, showed granules which were few in number and of large size. Cancer cells resembling in granule-appearances the cells of the corresponding normal columnar epithelium were entirely absent. The occurrence of granule-containing cells was quite irregular, but where the cancer cells still showed an arrangement around a lumen in a single approximately regular layer, one or two cells in the ring might show granules, while all the other cells around the lumen were completely devoid of them.

Similar observations obtain in the cases of carcinoma of the body of the uterus.

4. Sarcoma.—This class of malignant neoplasms is represented by only one example, viz. a case of melanotic sarcoma of the vulva. Here the great majority of the cells of new growth contained no granules of any kind; about one-sixth of the total number contained granules of melanin, and a very few showed Altmann-granules, distinguishable by their red colour from the brown pigment-granules. Here and there a cell contained both melanin and Altmann-granules.

5. Endothelioma.—In the cases of endothelioma granules were small and few in number (1 case) or altogether absent (2 cases). In the fourth instance, however, granules were numerous; this was a case of perithelioma in which islets of tissue, well-staining both as regards nuclei and granules, were embedded in a groundwork of necrotic tissue showing neither granules nor nuclear staining.

VI. CONCLUSIONS.

Although the number of cases of new growths dealt with so far is comparatively small (45), yet these present a considerable amount of variety, and the granule-appearances observed have been on the whole remarkably consistent for each group. As far as the present research has proceeded the following conclusions may be drawn:—

1. Most kinds of normal cell, after treatment by the author's modification of Altmann's method, contain granules.
2. The nature of the granules varies with the cell-species in which they occur, and indicates a method of classification of cells according to the micro-chemical reactions of their granules.
3. In inflammatory conditions granules are present in the various cell-species concerned.
4. In all innocent neoplasms examined granules were present in the cells.
5. In malignant new growths granules tend to disappear, or are absent altogether, from the particular type of cell involved.

CONTRIBUTION TO THE HISTOLOGY OF X-RAY DERMATITIS.

By C. W. ROWNTREE.

The microscopic appearances of human X-ray dermatitis have been studied by the examination of portions of skin which for various reasons had been exposed to X-rays for different periods.

In the case of human tissues it is obviously a difficult task to obtain for examination material in sufficient variety, and with a sufficiently exact history as to number and duration of exposures, to render anything like an adequate investigation possible, and generalisations—controlled by the results obtained in animal experiments—are therefore inevitable.*

Sections from certain of the cases dealt with will be described :—

1. A portion of scalp from the parietal region which had been subjected to several lengthy exposures in the course of the X-ray treatment of an inoperable sarcoma of the neck. The part examined was in no way affected by the growth, which had not ulcerated. The skin had become thinned, glazed, reddened, pigmented, and practically bald.

For purposes of comparison a portion of scalp from the corresponding part of the head of a bald old man was also examined.

Microscopical examination showed that the surface epithelium was slightly thinned, but otherwise unchanged.

Hairs were absent, but hair follicles were still present, though they had lost their normal structure and were represented by clumps of epithelial cells which beyond a slightly irregular arrangement were apparently not abnormal. In certain instances the connection of this mass of cells with the surface epithelium was very attenuated.

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* The animal experiments described in this paper were conducted by Dr. Lazarus-Barlow.

The sebaceous glands had entirely disappeared, while in the naturally bald skin they were very numerous.

In the corium there was an increase in the number of nuclei of the fixed connective-tissue cells, but there were no plasma cells or lymphocytes, either surrounding the atrophic hair follicles or elsewhere. There was a considerable increase in the number of pigment cells, and the superficial capillaries were much dilated.

The elastic-tissue network had undergone no noticeable change.

2. This was a portion of skin from the finger. The hand had been amputated for X-ray carcinoma. The naked-eye appearance of the skin was similar to that of the specimen just described.

Microscopically, the epithelium consists of some 8–10 layers of apparently normal cells. The papillary arrangement of the epidermis had disappeared entirely or was much diminished.

The superficial capillaries were dilated, and there was a very marked increase in the thickness of the deeper-lying vessels.

The corium is represented by a cellular connective tissue in which all the normal structures have disappeared.

There are no masses of plasma-cell or leucocytic infiltration, in fact the connective tissue approaches ordinary scar tissue in general appearance.

The destruction of the yellow elastic tissue is striking; there is a general disappearance from a narrow zone under the epidermis, but in addition this tissue has disappeared in an irregular patchy manner throughout the corium, in the same fashion as is seen in such conditions as lupus.

3. The next specimen to be described is a small tumour which developed on the dorsum of the hand of a man in whom a finger had been amputated for X-ray carcinoma.

The tumour was hemispherical in shape, and sprang abruptly from the surface, forming a dome-like swelling the size of half a cherry.

On microscopical examination it was found that the surface epithelium was stretched and thinned out, and over the summit of the swelling had disappeared and was represented by a layer of necrotic granulations.

The mass of the tumour was made up entirely of granulation tissue, of which the individual cells were large and well defined. A few multinucleated cells were present, but in no instance were more than three nuclei present. Very few plasma cells or leucocytes were detected.

Differential staining showed that the elastic-tissue network had entirely disappeared from the tumour itself, and that in the surrounding skin the sub-epithelial elastic-tissue plexus had also diminished or disappeared.

The presence of a lymph node in the sub-epithelial tissue quite close to the nodule was noted. There was some increase in the thickness of the vessel walls.

It is suggested that these specimens show a progressive series of changes in the two types of tissue present—epithelium and connective tissue.

On the one hand, in the epithelium are changes of a retrogressive nature, shown by the atrophy and disappearance of hair follicles and other epithelial appendages; on the other hand, changes in the connective tissue are of a formative nature, varying from the slightly increased cellularity met with in the first specimen to the formation of a well-marked connective tissue tumour in the last.

But, in addition to the above, other changes of a different nature occur in the epidermis of the hands of all who suffer from chronic X-ray dermatitis; that is to say, the formation of warts. These, however, differ from the common infective wart in that they are flatter, harder, and less localised overgrowths of epithelium.

The difference is still more striking on microscopic section, for instead of the attenuated and elongated papillæ clothed with epithelium which are characteristic of the ordinary wart, there is a disappearance of the papillæ, and replacing one or possibly several fused interpapillary epithelial processes is a large hemispherical mass of cells which projects downwards into the corium, pushing the normal structures in front of it. The pressure of this downwardly projecting mass of cells possibly accounts for the pain which is so constantly complained of in connection with these warts.

Another point of interest is that in these projecting masses of epithelium the normal slow gradation from the soft protoplasmic cells of the basal layer to the keratinized cells on the surface is, as it were, hurried over, and cells highly charged with keratin are met with only one or two layers removed from the basal membrane.

The accompanying diagrams show silhouettes of three such warts.

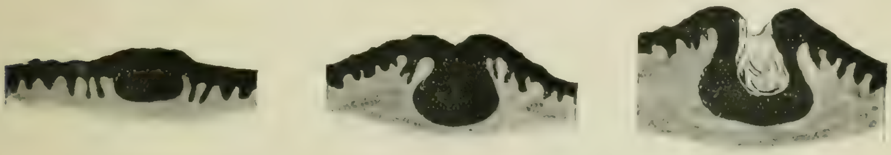

FIG 1

When, as in some of the sections, there is an infiltration of plasma cells below the projection and a rarefaction of the elastic-tissue network, it is obvious that the condition is not far removed from carcinoma. In point of fact it is next to impossible to distinguish clinically between a wart of perfectly simple character and one which has already passed the border line and is definitely infiltrating.

An experimental investigation of X-ray dermatitis was carried out by exposing animals to X-rays for varying periods.

In the early experiments rats and mice were used, and no precautions were taken to protect vital organs from exposure to the influence of the rays; with the result that all the animals died before any noteworthy changes in the skin had manifested themselves.

Ultimately a method already described (Arch. of Middlesex Hospital, 1908, Seventh Cancer Report) was adopted, whereby the tails of rats were exposed in such a way that the dorsal aspects of the tails alone were directly in the path of the rays, the ventral surface only receiving rays which had passed through the thickness of the tail. The lateral aspects of the tail would obviously receive an amount of rays intermediate between the dorsal and ventral surfaces.

At first, owing to the difficulty of accurately focussing the X-ray tubes on to the part it was desired to expose, the results varied considerably in different animals, but in the later experiments they were more constant.

Considerable doses had to be employed in order to obtain effects, which manifested themselves first of all in swelling and immobility of the tail, then in redness and desquamation of the epithelium, and finally in necrotic changes which were, however, confined to the dorsal surface of the tail at the proximal end; but at the distal end, where movement was more free, and where the tail was of course much thinner, all surfaces appeared equally affected, and actual gangrene occurred. Where there was necrotic change the sloughs were very dry, tough, and extremely tenacious; suppuration never attended their removal. In some cases where the tip of the tail sloughed the appearances suggested the probability of its resulting from vascular changes and not from direct destruction by the rays.

On microscopical examination of the tails, it was found that the transverse section presented three regions materially differing from one another:

(*a*) The *dorsal* surface, where in the majority of instances the surface epithelium was either disintegrated and infiltrated with small cells, or else had completely disappeared. In the corium were very striking changes: hairs, hair follicles, sebaceous glands, had already entirely disappeared, to be replaced

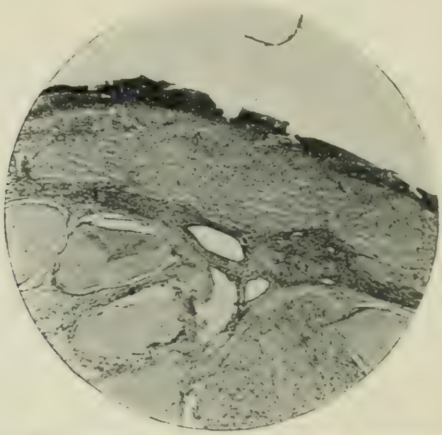

FIG. 2.—Microscopical appearance of dorsal surface of rat's tail after exposure to the rays.

by a cellular connective tissue, in which, however, wandering cells were not evident.

The sequence of events in the disappearance of these epidermal appendages appears to be firstly the shedding of the hairs, then the atrophy of the hair follicles and the neighbouring sebaceous glands, finally some change occurs in the cells, and they ultimately completely disappear.

(*b*) On the *ventral* surface there was practically no departure from the normal.

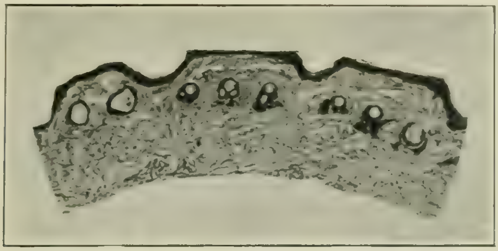

FIG. 3.—Microscopical appearance of ventral surface of rat's tail after exposure to the rays.

(*c*) The *intermediate* region on each side of the tail showed the most pronounced changes. Here the epidermis, instead of consisting of about 6–8 layers as in the normal tail, showed 10–12 layers ; and, moreover, this hypertrophic change was not confined to the epidermis, but was shown by the various epidermal appendages, the hair follicles forming large cellular masses which were very striking.

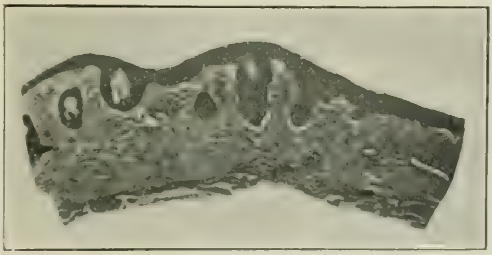

FIG. 4.—Microscopical appearance of "intermediate region" of rat's tail after exposure to the rays.

Other experiments were carried out by exposing the rabbit's ear to X-rays. In order to diminish the possibility of fatal injury, the head and body of the rabbit were enclosed in a leaden box, made to fit fairly accurately, but having small slits through which the ears could project.

The ears were laid flat on a wood block and kept in that position by superimposing a sheet of lead, in which, however, was a circular aperture through which the rays were applied to the ear.

Expt. I.—In this experiment the ear was exposed on two successive days, the total dose received being approximately equivalent to a Sabouraud pastille dose and a half.

In 14 days redness and desquamation appeared on the exposed area and the hair commenced to fall out. In 16 days desquamation was very marked, and in 18 days bullae appeared. In 20 days inflammation of the opposite side of the ear commenced and the hair fell out. In 30 days the hair had almost disappeared from both surfaces of the ear, and on the exposed surface there was a large ulcerated area covered with thick, hard, and tenacious scabs, which showed no tendency to separate.

A microscopical section of the edge of this area showed an almost complete disappearance of the various appendages of the skin on the dorsal surface, the covering epithelium being converted into a layer of necrotic tissue, which was in continuity with the living tissue without the intervention of as much granulation tissue as would be expected in similar lesions arising from other causes.

The ventral surface of the ear had undergone a striking change. The surface epithelium had become very considerably hypertrophied, and this hypertrophy had been shared in by the remains of the hair follicles, from which, of course, the hairs had disappeared. Sebaceous glands had entirely disappeared. The overgrowth of the epidermis and of the interpapillary processes and of the hair follicles was so considerable that careful examination was necessary to differentiate the condition from that of a malignant growth.

Expt. II.—In this experiment a dose equivalent to one pastille dose was given, but the hole in the lead sheet was covered with ordinary white filter paper.

No change was apparent for 15 days, and then slight redness of the skin appeared. On the 18th day the vessels were injected, and there was well-marked pigmentation of the exposed area. The hair had commenced to fall both from the dorsal and ventral surface. In 28 days the ear was like crinkled parchment, the surface quite hairless, glazed, shrivelled, and shrunken. It was noted that in those situations where the growth of hair was thickest, it commenced to fall later than in those parts where there was less.

Expt. III.—In this experiment the conditions were identical with the last, with the exception that aluminium foil about ·25 mm. thick was substituted for the filter paper used in the last experiment. The succession of events was the same up to a certain point, redness and pigmentation were marked—the latter perhaps more marked. The hair fell out, and the part became quite bald, but there was none of the atrophy and shrivelling seen in the last experiment, the skin undergoing no marked pathological change.

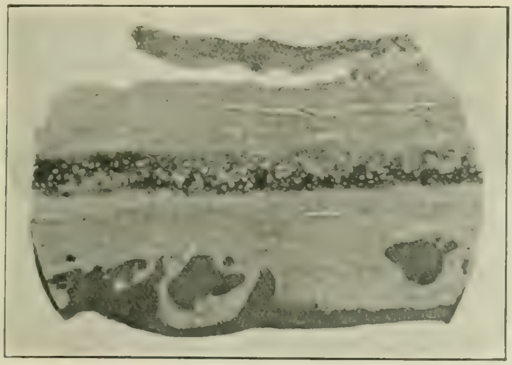

FIG. 5.—Microscopical appearance of whole thickness of rabbit's ear after exposure to the rays. Note the necrotic epithelium, which is separating, on the dorsal surface, and the marked hypertrophy and irregularity of that on the internal surface of the ear.

Microscopical examination of this specimen showed increase of pigment-bearing cells in the corium, and also an increase of the pigment in the deeper cells of the epidermis.

There was increased cellularity of the corium with the presence of a fair number of cells similar to the human plasma cell. The surface epithelium was slightly but uniformly hypertrophied, and the various epidermal appendages had to a slight extent shared in the change.

ON THE ACTION OF CERTAIN ANIMAL AND OTHER SUBSTANCES ON THE DEVELOPMENT OF THE OVA OF ASCARIS MEGALOCEPHALA.

(PRELIMINARY NOTE.)

BY W. S. LAZARUS-BARLOW AND SOMERVILLE HASTINGS.

IN this research is being investigated the action upon the ova of *Ascaris megalocephala*, exerted by certain substances which have been found by one of us to affect a photographic plate in the dark or the leak of an electroscope. Although our experiments must be considerably extended, the results so far are worthy of record.

Method.—Whereas the development oft he ova of *Ascaris megalocephala* at room temperatures is such that about 80 per cent. of the ova will have passed into the two-cell stage in perhaps 24 hours, at 5°C. a similar condition is a matter of months. While some of the earlier experiments were carried out at the room temperature, the later were conducted uniformly at a temperature of about 8°C. At this temperature about 40 per cent. of the ova will have passed into the two-cell stage in a week. To maintain this constant low temperature the following method was devised:—A rectangular wooden box with one of the shorter sides replaced by a metal plate, and with a hinged lid, was arranged, with the metal plate downward, over an ordinary incandescent electric bulb. The box was supported on a retort stand, in order that the distance between the lamp and the metal plate might be varied at will. In the box was fixed a maximum and minimum thermometer and shelves on which the ova, enclosed in Petri dishes, could be placed. The whole apparatus was kept in the cold storage chamber, the temperature of which is maintained at a little below freezing point. By varying the distance between the box and the electric lamp it was found that any temperature between 3°C. and 10°C. could be maintained with very slight variation.

Fresh female specimens of *Ascaris megalocephala* were obtained from the horse-slaughterer. The terminal half-inch of each oviduct was removed, the contained ova squeezed out and carefully mixed together. Thin films of the ova were spread on the centres of two-inch coverslips, and to prevent desiccation were covered with a thin layer of $1\frac{1}{2}$ per cent. agar in 4 per cent. solution of boric acid, cooled to just above its solidifying point before being poured on the ova. It had previously been found that the influence of boric acid in this strength on the development of the ova is negligible, if not entirely absent, while it prevents the growth of bacteria when the experiment is prolonged.

Ordinary microscopic slides, at the two ends of which small strips of glass had been cemented with marine glue, served as supports for the coverslips carrying the ova. On the glass base a thin layer of the substance under observation was spread, so that the ova on the coverslip were separated from the substance on the slide by a distance of $\frac{1}{32}$ to $\frac{1}{16}$ inch, and were nowhere in contact. When liquid extracts were used for experiment well slides were employed; and to prevent any possibility of the fluid or moistened solid substance rising by capillary attraction to the coverslip and ova, a small quantity of paraffin wax was melted into the angles between the slides and supports.

In all cases experiment and control observations were made under identical conditions, even to their enclosure side by side in the same Petri dish. A moist atmosphere was maintained by placing a piece of wet blotting-paper on the bottom of the Petri dish. Where the substance under observation was deliquescent it was found best to moisten it before the experiment, and where a liquid was being examined some water was placed in the well of the supporting slide in the control. Every day both experiment and control were examined, and a minimum of 200 ova counted in each, so that the relative numbers of undivided, two-cell, and more-than-two-cell forms were estimated. Hitherto the development of ova as far as the formation of living worms has not been followed in these experiments. To obtain constant results it was found necessary to pay the greatest possible attention to the exactness of detail as described. Replacement of glass (a dielectric) by iron, for example, considerably modified the results. Evidence of a similar action has been found by one of us in another direction.

Substances used for Experiment.—At present we are in a position to record results with the following substances alone, all of which exert a profound effect on a photographic plate in the dark.

(*a*) Watery extract of liver of the sheep. (Specimen prepared 24/3/08.)
(*b*) Watery extract of the testis of the herring. (Six samples mixed.)
(*c*) Watery extract of the ovary of the herring. (Six samples mixed.)

The above extracts were protein-free and prepared by the method described by one of us on page 139 of the seventh volume of Cancer Reports (Arch. Middlesex Hospital).

The extracts (which contained free acetic acid) were evaporated to dryness at 45°C. to expel most of the acid, and then taken up with water. Even after this treatment the extract remained slightly acid to litmus, but that the effect on the development of the ova was not due to the free acid present was shown by the facts (1) that the neutralised extracts also possessed the same effects as the unneutralised :* and (2) that extracts of different organs prepared in an exactly similar manner led in some cases to acceleration of the development of the ova, and to retardation in others.

(*a*) **Watery Extract of Liver of Sheep.**—Ten different experiments with this substance were made, and 30 day-to-day observations made of its action upon the ova. In 2 of these the slight acidity remaining after evaporation to dryness at

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* The photographic effect described by one of us in the last volume of these Cancer Reports is still present when the extract prepared as above is neutralised. It is also given by the liquid extract as well as by the extract evaporated to dryness.

55° C. was neutralised. On 22 occasions retarded development of the experimental ova, as compared with the control, was observed; on one occasion the 2 were equal, and on 7 there was acceleration. With one exception the 10 experiments showed initial retardation, whatever the subsequent course of development. Below are given two typical examples, the actual totals being reduced to 200 in each case to facilitate comparison.

Experiments showing the Effect of Exposure to Watery Extract of Sheep's Liver upon the Development of the Ova of Ascaris Megalocephala.

Date.		EXPERIMENT I. Temperature 8° C.		EXPERIMENT II. Room Temperature (18° C.).		
	—	1-Cell Stage.	2-Cell Stage.	1-Cell Stage.	2-Cell Stage.	Over-2-Cell Stage.
Feb. 5	Experiment	200	0	200	0	0
	Control -	200	0	200	0	0
„ 6	Experiment	199	1	39	143	18
	Control -	198	2	27	156	17
„ 7	Experiment	196	4	29	27	144
	Control -	187	13	8	43	149
„ 9	Experiment	153	47	37	14	149
	Control -	137	63	11	11	178
„ 10	Experiment	132	68	50	5	145
	Control -	127	73	8	5	187
„ 11	Experiment	121	79	30	9	161
	Control -	119	81	11	9	180
„ 13	Experiment	69	131	—	—	—
	Control -	70	130	—	—	—

(b) **Watery Extract of Testis of Herring.**—Three different samples of this substance were examined, and 10 day-to-day observations made. In 9 of these *accelerated* development of the experimental ova, as compared with the control, was observed, and in only 1 was there retardation. In all instances the initial effect was acceleration.

(c) **Watery Extract of Ovary of Herring.**—Five different samples were examined, and 17 day-to-day observations made.

In 14 of these *retarded* development of the experimental ova, as compared with the control, was observed; in 1 the rates of development were equal, and in 2 acceleration occurred. In 4 instances the initial effect was retardation, in the fifth the initial change was a very slight acceleration. Below are given experiments indicating the above points.

EXPERIMENTS SHOWING THE EFFECT OF EXPOSURE TO WATERY EXTRACTS OF (I.) TESTIS AND (II.) OVARY OF HERRING UPON THE DEVELOPMENT OF THE OVA OF ASCARIS MEGALOCEPHALA.

Day of Experiment		I.—TESTIS. Temperature 8° C.			II.—OVARY. Temperature 8° C.		
	—	1-Cell Stage.	2-Cell Stage.	Over-2-Cell Stage.	1-Cell Stage.	2-Cell Stage.	Over-2-Cell Stage.
1	Experiment	200	0	—	200	0	—
	Control -	200	0	—	200	0	—
2	Experiment	160	40	—	196	4	—
	Control -	183	17	—	194	6	—
3	Experiment	132	68	—	176	24	—
	Control -	153	47	—	169	31	—
4	Experiment	78	122	—	162	38	—
	Control -	84	116	—	154	46	—
5	Experiment	52	148	—	106	94	—
	Control -	60	140	—	95	105	—
6	Experiment	23	78	99	57	137	6
	Control -	27	87	86	49	146	5

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